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ORIGINAL ARTICLE

# Effect of periodontal therapy on glycemic control and circulating TNF-α in type 2 diabetic patients

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**Abstract** Studies suggest that elevated circulating tumour necrosis factor- α (TNF- α) may contribute to insulin resistance in patients with type 2 diabetes. The source of plasma TNF has been thought to be adipocytes associated with obesity, but inflammation and infection result in TNF- α production as well. The present study was a randomized controlled clinical trial to evaluate the role of periodontal treatment in glycemic control and its relationship with the inflammatory marker TNF-α in type 2 diabetic subjects with chronic generalized periodontitis. In total, 30 patients were enrolled in the study. The selected patients were randomly assigned into two groups (group A and B) comprising of fifteen patients each. Patients who refused periodontal treatment were automatically placed in the control group; others were randomly assigned to either treatment or control group. Group A (Treatment group) which received treatment with full mouth scaling and root planing followed by systemic Doxycycline (100 mg daily for 14 days) and Group B (Control group) which received no treatment. The plaque index, gingival index, probing depth, clinical attachment loss, HbA1c value, and circulating TNF- α concentrations were measured at baseline and three months after the non-surgical periodontal therapy in both the treatment and control groups. All periodontal parameters, serum TNF- α levels and HbA1c levels were significantly decreased three months after the nonsurgical periodontal therapy compared to the baseline values in the treatment group where as there was no significant change in the control group. The study results indicated that periodontal treatment could be undertaken along with the standard measures for the diabetic patient care and prevention, and control of periodontal disease must be considered as an integral part of diabetes control.

**Keywords** Periodontal therapy · TNF-α · HbA1c · Type 2 diabetes mellitus

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## Introduction

Evidence is increasing that oral health has important impacts on systemic health. Among those, the link between periodontal disease and Diabetes Mellitus has gained considerable attention. Diabetes Mellitus encompasses a heterogeneous group of disorders with the common characteristic of altered glucose tolerance or impaired lipid and carbohydrate metabolism [1]. The clinical manifestations in Diabetes Mellitus are related to the complications of diabetic hyperglycemic state either directly or indirectly [2]. Periodontitis has been proposed as the sixth classic complication of Diabetes Mellitus and regarded as a risk factor for diabetic decompensation [3].

Although periodontal disease is the result of an interaction between microbial plaque and the resultant inflammatory and immunological changes within the periodontal tissues, it is also recognized that the nature and severity of this interaction in turn may be modified by many systemic factors, including hormonal changes, nutritional deficiencies, blood dyscrasias, drug ingestion, aging or a compromised immune system.

Among the systemic factors, the relationship between periodontal disease and Diabetes mellitus has been studied extensively. Many investigators, in their epidemiological, experimental and clinical studies have reported that the severity of periodontal disease is significantly greater among patients with diabetes than in patients without Diabetes mellitus.

The influence of Diabetes Mellitus on periodontal health has been well established. A complex two way relationship exists between Diabetes Mellitus and Periodontitis creating a vicious cycle that exacerbates both diseases when present in the same individual [4].

Evidence exist which support the adverse effects of periodontal infection on glycemic control. The main mechanism responsible for the two way relationship between Diabetes mellitus and Periodontitis is the large secretion of inflammatory mediators which influence glucose and lipid metabolism [5]. Of these inflammatory markers, Tumor Necrosis Factor Alpha (TNF-α) plays a significant role and also has a role in insulin resistance. TNF-α, a proinflammatory cytokine produced by adipose tissues, plays a predominant role in inducing insulin resistance in obese subjects [6]. In addition, researchers have hypothesized that TNF-α levels in the circulation of diabetic subjects are influenced by periodontal infection and inflammation [7].

Therefore, it has been conjectured that periodontal therapy may improve the metabolic control of Diabetes Mellitus via improved insulin sensitivity by reducing the peripheral TNF-α concentration [6].

Hence, the purpose of this study is to assess the role of periodontal therapy in glycemic control and reduction of the inflammatory marker TNF-α.

## Materials and methods

- For carrying out the proposed study, thirty patients who reported to the diabetes clinic of School of Tropical medicine, Kolkata, INDIA as well as the Department of Periodontics, Dr. R. Ahmed Dental College and Hospital, Kolkata, INDIA were included in the study irrespective of sex and religion. The selected patients were randomly assigned into two groups (group A and B) comprising of fifteen patients each. Group A was the treatment group and Group B was the control group. Patients who refused periodontal treatment were automatically placed in the control group; others were randomly assigned to either treatment or control group.

Group A received treatment with full mouth scaling and root planing followed by systemic Doxycycline (100 mg daily for 14 days). Group B received no treatment (control group).

The procedure was explained in detail to patients and they were included in the study after obtaining their written informed consent. Patients were informed that they could withdraw from the study at any time for any reason. The study protocol described herein was approved by the college ethical committee concerning the use of human subjects in clinical experimentation.

Inclusion criteria for selection of patients

- Patients >30 years, both males and females.
- Chronic generalized periodontitis patients (Armitage criteria) [8]
- Patients diagnosed with type 2 diabetes mellitus (HbA1c 7.5–11 %) [9]
- No major diabetic complications.
- Patient willing to take part in the study and maintain appointment regularly.

Exclusion criteria

- Patients suffering from any other systemic diseases.
- Present and past smokers.
- Patients who have undergone periodontal treatment 6 months prior to the study.
- Pregnant or lactating mothers.
- Patients who have received any antibiotics for the last 3 months.
- Less than 16 remaining natural teeth.
- Physician's consent and details of patient's diabetes control was obtained and no change in the medication or diet was made for the patients. None of the patients received any additional guidance in managing their diabetic status. All the multiple variables like diet, exercise and diabetic management were kept constant. After oral examination the teeth with poor prognosis were extracted. Patients requiring antibiotics post extraction were taken up for the study after the period of 3 months. Patients were instructed to report to the Department of Periodontics after overnight fasting (8 h duration). Under aseptic conditions venous blood was drawn from ante-cubital fossa using Vacutainers (BD vacutainer)™. The collected blood samples were transported to the Pathology laboratory for the estimation of Fasting blood sugar (FBS), and Glycated haemoglobin (HbA1c), by High Pressure Liquid Chromatography. One sample was carried to the Department of

Pathology and Transfusion Medicine, Peerless Hospital & B.K.ROY Research Centre, Kolkata; it was centrifuged at 3,000 rpm for 5 min and stored in eppendorf microcentrifuge tubes (Sigma-Aldrich Chemical Company, USA) at −20 °C for subsequent estimation of serum TNF-α by ELISA. A RayBio Human TNF-α ELISA kit (Assaypro, USA) was used for the study and the readings were obtained by an ELISA reader (Sunrise micro plate reader, Tecan, Switzerland). These were recorded at baseline (day zero) and at the end of 3 months.

A digital orthopantomogram was advised for all the patients. For periodontal status of the two groups (group A and group B) following parameters were recorded after collection of blood samples:

- Plaque index according to Silness and Loe (1964) [10]
- Gingival index according to Loe and Silness (1963) [11]
- Probing pocket depth [12]
- Clinical attachment level [12]

Four units of each teeth i.e. distofacial, facial, mesiofacial, and lingual surfaces were examined and recorded. The parameters were recorded at baseline (day zero), and at the end of 3 months.

Impressions of the upper and lower arches were made using alginate impression material and casts were poured in dental stone. Acrylic stents were made with cold cure acrylic resin on each patient's cast to fit over the occlusal one third of the teeth. A groove was made in the acrylic stent to standardize the point of entry to the pocket during recall visits. The depth of the pocket was measured using UNC-15 graduated Probe (Hu-Friedy, USA). Probing pocket depths (PPD) were measured to the nearest millimeter from the gingival margin with calibrated periodontal probe (UNC-15 graduated Probe). The pocket depth was measured at 4 sites per tooth (mesiofacial, facial, distofacial and lingual). In the present study the Ramjford method was used to determine the clinical attachment level. (CAL) All the subjects underwent periodontal examination by a single previously calibrated investigator. The difference in the clinical and laboratory indices between Group A and B is depicted in Tables 1 and 2.

After recording the periodontal status, patients in Group A were given oral hygiene instructions and underwent full mouth scaling and root planing procedure performed under local anesthesia. Scaling and root planing was performed by the principal investigator using ultrasonic scalers and hand instruments while the subjects were under local anesthesia. The schedule of the visit was once a week for 1 month. On recall visit after 3 months, supragingival plaque was removed, and oral hygiene instructions were reinforced as required. Additionally these patients were placed on Doxycycline 100 mg, two tablets for first day, then one tablet daily for total of 14 days [13]. For control group (Group B) full mouth scaling and root planing was not performed and oral hygiene instructions were not given. After completion of the study, these patients were given a full non-surgical and supportive periodontal treatment if needed. Patients were recalled and periodontal status was again recorded at the end of 3 months. The blood samples were again collected at the end of 3 months for measuring the metabolic parameters as well as the biochemical parameter TNF-α for the study.

The data was checked for normal distribution by "Kolmogorov-Smirnov goodness-of-fit test". Following statistical methods were implied in the present study:

1. Paired "t" test: It was used to compare the various parameters at baseline and after 3 months within the same group.
2. Student's unpaired "t" test or the Independent sample "t" test: It was used to compare the various parameters between the groups A and B.

   Level of significance for both the above mentioned statistical tests was considered at 5 % ($p$ value $< 0.05$).
3. Pearson's product moment correlation: It was used to correlate the various clinical, metabolic and immunological parameters at the baseline as well as after 3 months.

   All the statistical calculations were done through Statistica version 6 [Tulsa, Oklahoma: Stat Soft Inc., 2001] and MedCalc version 11.6 [Mariakerke, Belgium: MedCalc Software, 2011].

## Results

Out of the 30 subjects included in the study, 17 were males and 13 were females. The mean age of the included subjects was 49.96 years. Out of the 30 patients, 4 subjects were only on sulfonylurea, 2 were without any medication and the remaining patients were on a combination of sulfonylurea and biguanides along with exercise and diet as the basic diabetic treatment. The descriptive statistics of Group A and Group B are indicated in Table 1 and 2.

Subjects in Group A showed a significant decrease in all the periodontal parameters namely mean plaque index scores, mean gingival index scores, mean probing pocket depth(PPD) values as well as clinical attachment levels (CAL) after 3 months compared to baseline values. These subjects also showed significant improvement in glycemic control, significant reduction in serum TNF-α levels as well as fasting blood glucose levels 3 months post therapy as compared to baseline. (Table 3) Contrary to Group A, Group B showed an insignificant change in all the periodontal, metabolic as well as immunological parameters.

**Table 1** Descriptive statistics of numerical variables – Group A [*n*=15]

| | Valid N | Mean | Median | Minimum | Maximum | Lower Quartile | Upper Quartile | Std. Dev. | Standard Error |
|---|---|---|---|---|---|---|---|---|---|
| HbA1c Pre | 15 | 65(8.13) | 64(8.0) | 54(7.1) | 83(9.7) | 62(7.8) | 69(8.5) | 7.68(0.67) | 2.93(0.17) |
| HbA1c Post | 15 | 56(7.31) | 55(7.2) | 46(6.4) | 70(8.6) | 52(6.9) | 62(7.8) | 6.53(0.60) | 2.53(0.15) |
| FBG Pre | 15 | 153.6267 | 156.2000 | 130.0000 | 170.0000 | 140.0000 | 164.2000 | 13.02412 | 3.362814 |
| FBG Post | 15 | 145.4667 | 150.0000 | 124.0000 | 160.0000 | 138.0000 | 154.0000 | 11.17310 | 2.884881 |
| TNF-α Pre | 15 | 10.9820 | 12.5000 | 4.8400 | 16.0000 | 7.4000 | 13.6000 | 3.63513 | 0.938588 |
| TNF-α Post | 15 | 7.8533 | 7.8700 | 2.7100 | 12.7900 | 6.8100 | 9.3000 | 2.45718 | 0.634441 |
| PI Pre | 15 | 1.7893 | 1.6000 | 1.2400 | 3.0000 | 1.4000 | 2.2000 | 0.51491 | 0.132950 |
| PI Post | 15 | 0.9467 | 0.8000 | 0.4000 | 1.6000 | 0.6000 | 1.2000 | 0.39437 | 0.101825 |
| GI Pre | 15 | 1.7407 | 1.8000 | 1.0600 | 2.2000 | 1.6000 | 2.0000 | 0.28999 | 0.074874 |
| GI Post | 15 | 0.4993 | 0.5000 | 0.1000 | 0.8000 | 0.3000 | 0.6000 | 0.21238 | 0.054837 |
| PPD Pre | 15 | 3.2500 | 3.5000 | 2.0000 | 4.4000 | 2.5000 | 3.9000 | 0.77367 | 0.199762 |
| PPD Post | 15 | 2.1907 | 2.1000 | 1.6000 | 3.0000 | 1.8000 | 2.6000 | 0.45052 | 0.116322 |
| CAL Pre | 15 | 4.1067 | 4.5000 | 2.0000 | 6.1000 | 3.1000 | 5.0000 | 1.21976 | 0.314940 |
| CAL Post | 15 | 3.6273 | 3.9000 | 1.2000 | 5.6000 | 2.8100 | 4.6000 | 1.24765 | 0.322142 |

(Table 4) Intergroup comparison of the post treatment values showed the decrease in all the clinical, metabolic and immunological parameters to be highly significant for group A. (Table 5) Using Pearson's correlation analysis, at baseline, serum TNF-α showed a strong positive correlation with HbA1c (*r* value + 0.86), probing pocket depth (*r* value + 0.78) and clinical attachment level (*r* value + 0.69) in Group A. There was a fair correlation between serum TNF-α and gingival index at baseline (*r* value + 0.40). After 3 months post therapy, serum TNF-α showed a strong positive correlation with HbA1c (*r* value + 0.83) and clinical attachment level (*r* value + 0.80). Serum TNF-α showed a good correlation with probing pocket depth (*r* value + 0.67). There was a negative correlation with gingival index (*r* value −0.11), 3 months post therapy.

## Discussion

The results of the present study demonstrated a significant improvement of glycemic control in the subjects of the study group (Group A) at 3 months post therapy. A statistically significant decrease in HbA1c level (0.82 %) was observed in the study group. Similar observations were reported by Kiran et al.; who examined the effect of periodontal therapy

**Table 2** Descriptive statistics of numerical variables – Group B [*n*=15]

| | Valid N | Mean | Median | Minimum | Maximum | Lower Quartile | Upper Quartile | Std. Dev. | Standard Error |
|---|---|---|---|---|---|---|---|---|---|
| HbA1c Pre | 15 | 65(8.09) | 63(7.9) | 53(7.0) | 78(9.3) | 58(7.5) | 74(8.9) | 8.35(0.76) | 2.94(0.197) |
| HbA1c Post | 15 | 66(8.16) | 64(8.0) | 54(7.1) | 79(9.4) | 60(7.6) | 73(8.8) | 7.63(0.74) | 2.83(0.190) |
| FBG Pre | 15 | 157.3467 | 158.0000 | 128.0000 | 186.2000 | 140.0000 | 168.000 | 17.77807 | 4.590278 |
| FBG Post | 15 | 157.9333 | 160.0000 | 130.0000 | 188.0000 | 142.0000 | 170.000 | 17.44160 | 4.500000 |
| TNF-α Pre | 15 | 10.0807 | 11.0000 | 6.1900 | 13.5100 | 8.1200 | 12.5000 | 2.46812 | 0.637266 |
| TNF-α Post | 15 | 10.0380 | 11.1000 | 6.3600 | 13.5800 | 8.1800 | 11.9400 | 2.39450 | 0.618257 |
| PI Pre | 15 | 1.4580 | 1.3000 | 0.4300 | 2.3000 | 1.2400 | 1.9000 | 0.47630 | 0.122980 |
| PI Post | 15 | 1.4173 | 1.2400 | 0.4300 | 2.2000 | 1.2000 | 2.0000 | 0.49743 | 0.128436 |
| GI Pre | 15 | 1.8133 | 1.8000 | 1.4000 | 2.3000 | 1.6000 | 2.0000 | 0.25875 | 0.066809 |
| GI Post | 15 | 1.8467 | 1.9000 | 1.5000 | 2.4000 | 1.6000 | 2.0000 | 0.23865 | 0.061618 |
| PPD Pre | 15 | 3.3200 | 3.4000 | 2.2000 | 4.2000 | 2.8000 | 3.7500 | 0.59336 | 0.153204 |
| PPD Post | 15 | 3.3907 | 3.5000 | 2.2000 | 4.4000 | 2.8000 | 4.1000 | 0.72104 | 0.186171 |
| CAL Pre | 15 | 4.1520 | 4.2000 | 2.5000 | 5.6800 | 3.4000 | 4.9000 | 0.95228 | 0.245879 |
| CAL Post | 15 | 4.2233 | 4.1000 | 2.5000 | 5.8000 | 3.3500 | 5.0000 | 1.00692 | 0.259985 |

*HbA1c* glycated hemoglobin mmol/mol (%), *FBG* fasting blood glucose, (mg/dl), *TNF-α* tumour necrosis factor alpha, (pg/ml), *PI* plaque index, *GI* gingival index, *PPD* probing pocket depth in mm, *CAL* clinical attachment level in mm

**Table 3** Comparison of baseline and 3-month HbA1c values, TNF-α levels, and periodontal parameters in group A after periodontal therapy

| Parameters | Baseline | 3rd month | *t*-value | *p* value |
|---|---|---|---|---|
| HbA1c % | 65.5±7.68 (8.13±0.67) | 56.33±6.53 (7.31±0.60) | 3.523 (13.97) | 0.000 |
| TNF-α (pg/ml) | 10.98±3.63 | 7.85±2.46 | 7.20 | 0.000 |
| FBS (mg/dl) | 153.63±13.02 | 145.47±11.17 | 5.46 | 0.000 |
| PI | 1.79±0.51 | 0.95±0.39 | 6.22 | 0.000 |
| GI | 1.74±0.29 | 0.499±0.21 | 16.67 | 0.000 |
| PPD (mm) | 3.25±0.77 | 2.19±0.45 | 9.82 | 0.000 |
| CAL (mm) | 4.11±1.22 | 3.63±1.25 | 7.93 | 0.000 |

with systemic Doxycycline on periodontal health and glycemic control of individuals suffering from type 2 Diabetes Mellitus [14]. A control group of patients with Diabetes Mellitus with similar periodontal status received no periodontal treatment as in the present study. Improvement of glycemic control with a reduction in mean HbA1c value (0.8 %) was reported to be statistically significant [14]. It was suggested that the improvement in the HbA1c values was possibly due to the reduction in the GI and bleeding on probing (BOP) values.

Subjects of the control group in the present study showed negligible increase in HbA1c value after 3 months while in the study of Kiran et al., there was no change in the control group. In 2001, Iwamoto et al. reported a slight reduction in plasma HbA1c level (0.8 %) in a group of 13 Japanese subjects with type 2 Diabetes mellitus [15]. Grossi et al. conducted a research involving type 2 Diabetes mellitus subjects with severe Periodontitis and treated them with scaling & root planing, subgingival irrigation ($H_2O$, Chlorhexidine, povidone iodine plus placebo or doxycycline- 100 mg daily for 14 days). A significant reduction in HbA1c levels was reported in subjects receiving doxycycline compared to placebo treated group [13]. These observations were in accordance with the present study. Rodrigues et al. also reported similar statistically significant reduction in HbA1c level after periodontal therapy in type 2 Diabetes mellitus patients with Chronic Periodontitis, but instead of doxycycline, amoxicillin/clavulanic acid as an adjunct to mechanical debridement was used [16]. Based on the study by Grossi et al. [13], systemic doxycycline 100 mg for 14 days was used as an adjunct therapy along with scaling and root planing in the present study. Promsudthi et al. reported a reduction in HbA1c level after periodontal therapy, but contrary to other studies, this decrease was not statistically significant [9]. Similarly, Dag et al. also observed a non significant decrease in HbA1c values after periodontal therapy [17]. Most of the previously undertaken studies incorporated non diabetic patients as control group and hence could not arrive at a definitive conclusion. Therefore to determine the relative contribution of periodontal therapy on glycemic control, the present study was designed to include type 2 Diabetes mellitus subjects with Chronic Periodontitis as control group that did not receive any periodontal treatment during the study period. In contrast to the findings of the present study, Christgau et al. reported that periodontal therapy did not affect the levels of HbA1c in uncontrolled diabetic subjects (i.e. HbA1c > 7 %) [18]. Westfelt et al. also claimed that HbA1c levels did not change with mechanical periodontal therapy [19]. Similar results were obtained by Patricia et al. [20] Current researches indicated lack of consensus as to whether non surgical therapy contributed to improvement in the glycemic control [14, 21].

Mechanical scaling and root planing are very essential for removal of plaque and calculus for reduction of inflammation as type 2 diabetics have an increased susceptibility to inflammation [22]. Hence, the therapy led to a 71.2 % reduction in the mean gingival index, 32.6 % reduction in the mean probing pocket depth and 11.7 % gain in the mean clinical attachment in the present study. These improvements were reflected at the systemic level by alterations in the serum TNF-α as well as reduction in glycated hemoglobin.

It has been believed that periodontal infection related TNF-α contributes to systemic inflammatory reaction. TNF-α is believed to be released from adipocytes and caused

**Table 4** Comparison of baseline and 3-month HbA1c values, TNF-α levels, and periodontal parameters in group B

| Parameters | Baseline | 3rd month | *t*-value | *p* value |
|---|---|---|---|---|
| HbA1c % | 64.93±8.35 (8.09±0.76) | 66.2±7.63 (8.16±0.74) | −0.435 (−2.00) | 0.065 |
| TNF-α (pg/ml) | 10.08±2.47 | 10.04±2.39 | 0.70 | 0.494 |
| FBS (mg/dl) | 157.35±17.78 | 157.93±17.44 | −1.13 | 0.279 |
| PI | 1.46±0.48 | 1.42±0.497 | 1.88 | 0.081 |
| GI | 1.81±0.26 | 1.85±0.24 | −1.58 | 0.136 |
| PPD (mm) | 3.32±0.59 | 3.39±0.72 | −1.27 | 0.223 |
| CAL (mm) | 4.15±0.95 | 4.22±1.01 | −2.07 | 0.058 |

**Table 5** Comparison of numerical variables between groups A and B – Student's unpaired *t* test ($p<0.05$)

| | Mean A | Mean B | *t*-value | df | p | Valid N A | Valid N B | Std. Dev. A | Std. Dev. B |
|---|---|---|---|---|---|---|---|---|---|
| HbA1c Pre | 65(8.13) | 65(8.09) | 1.10(0.152) | 28 | 0.879865 | 15 | 15 | 7.68(0.67) | 8.35(0.76) |
| HbA1c Post | 56(7.31) | 66(8.16) | −3.74(−3.446) | 28 | **0.0018** | 15 | 15 | 6.53(0.60) | 7.63(0.74) |
| FBG Pre | 153.6267 | 157.3467 | −0.6537 | 28 | 0.518608 | 15 | 15 | 13.02412 | 17.77807 |
| FBG Post | 145.4667 | 157.9333 | −2.331 | 28 | **0.0272** | 15 | 15 | 11.17310 | 17.4416 |
| TNF-α Pre | 10.9820 | 10.0807 | 0.7945 | 28 | 0.433595 | 15 | 15 | 3.63513 | 2.46812 |
| TNF-α Post | 7.8533 | 10.0380 | −2.4661 | 28 | **0.020046** | 15 | 15 | 2.45718 | 2.39450 |
| PI Pre | 1.7893 | 1.4580 | 1.8295 | 28 | 0.077994 | 15 | 15 | 0.51491 | 0.47630 |
| PI Post | 0.9467 | 1.4173 | −2.8716 | 28 | **0.007697** | 15 | 15 | 0.39437 | 0.49743 |
| GI Pre | 1.7407 | 1.8133 | −0.7241 | 28 | 0.474982 | 15 | 15 | 0.28999 | 0.25875 |
| GI Post | 0.4993 | 1.8467 | −16.3341 | 28 | **0.000000** | 15 | 15 | 0.21238 | 0.23865 |
| PPD Pre | 3.2500 | 3.3200 | −0.2781 | 28 | 0.783011 | 15 | 15 | 0.77367 | 0.59336 |
| PPD Post | 2.1907 | 3.3907 | −5.4664 | 28 | **0.000008** | 15 | 15 | 0.45052 | 0.72104 |
| CAL Pre | 4.1067 | 4.1520 | −0.1135 | 28 | 0.910476 | 15 | 15 | 1.21976 | 0.95228 |
| CAL Post | 3.6273 | 4.2233 | −1.4397 | 28 | **0.161031** | 15 | 15 | 1.24765 | 1.00692 |

insulin resistance together with obesity [23]. Researchers have also suggested that TNF-α impairs insulin signaling by increasing the adiposity secretion of free fatty acids [17]. Researchers agreed that this process strengthened glycemic control by raising insulin resistance in diabetic patients and this hypothesis suggested that periodontal therapy could effectively improve glycemic control by decreasing proinflammatory mediators. Yang et al. found a significant reduction in serum TNF-α, HbA1c and periodontal parameters following periodontal therapy in the treatment group consisting of type 2 Diabetes mellitus patients with Chronic Periodontitis. They suggested that periodontal therapy could effectively reduce HbA1c levels by reducing circulatory TNF-α concentration [24]. Similar observations were made by Iwamoto et al. [15, 25] and Dag et al. [17] In the present study, a significant decrease in the serum TNF-α level (10.98±3.63 pg/ml at baseline to 7.85±2.46 pg/ml) was obtained in the study group (Group A) which is in accordance with the observations reported in the previously mentioned studies. In contrast to the above findings, Kardesxler et al. and Yamazaki et al. reported that increased TNF-α was associated with inflammatory periodontal disease, but significant post treatment reduction in TNF-α was not observed by them [26, 27].

However, Talbert et al. reported an increase in TNF-α level after periodontal treatment [22]. Nishimura et al. suggested that Periodontitis raised serum TNF-α level and affected insulin resistance [6]. In agreement with this suggestion, the determination of positive correlation between TNF-α and probing pocket depth (PPD) and TNF-α and gingival index (GI) in this study were compatible showing a correlation between TNF-α and Periodontitis. Serum TNF-α values were correlated with HbA1c as well as with the periodontal parameters in the present study (i.e. GI, PPD & CAL). A positive correlation was found between them and hence this study supported the hypothesis that the better glycemic control obtained after periodontal treatment in the study group was due to reduction of gingival index and bleeding on probing brought about by reduction in the inflammatory mediators, including TNF-α. Reduction in all the clinical parameters in the present study supported the observation of Engebretson et al. who claimed a positive correlation between TNF-α and clinical attachment levels and Bretz et al. who showed correlation between TNF-α and severe Periodontitis [28, 29].

The main limitation of the present study was the small number of patients incorporated within the study and a small follow up period. The follow up period could not be extended as the control groups of subjects were also Type 2 Diabetes mellitus patients with Chronic Periodontitis, and hence it would have been ethically unacceptable to defer periodontal treatment in these patients for a longer period. Also the possibility that the observed improvements in glycemic control and in the reduction of serum TNF-α might be due to diet, was not controlled in the present study.

## Conclusion

The overall results showed that non surgical periodontal therapy resulted in significant improvement of glycemic control along with significant reduction in serum TNF-α in all the subjects of the treatment group (Group A). The study results indicated that periodontal treatment can be undertaken along with the standard measures for the diabetic patient care and prevention, and control of periodontal disease might be considered as an integral part of glycemic control of type 2 diabetic subjects.

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## References


1. Diabetes and periodontal diseases [position paper]. J Periodontol 2000; 71:664–678.
2. Lalla E, Lamster IB, Drury S, Fu C, Schmidt AM. Hyperglycemia glycoxidation and receptor for advanced glycation end products: potential mechanisms underlying diabetic complications, including diabetes – associated periodontitis. Periodontology 2000. 2000;23: 50–62.
3. Löe H. Periodontal disease. The sixth complication of diabetes mellitus. Diabetes Care. 1993;16(1):329–34.
4. Navarro-Sanchez AB, Faria-Almeida R, Bascones-Martinez A. Effect of non-surgical periodontal therapy on clinical and immunological response and glycaemic control in type 2 diabetic patients with moderate periodontitis. J Clin Periodontol. 2007;34(10):835–43.
5. Taylor GW. The effects of periodontal treatment on diabetes. J Am Dent Assoc. 2003;134 Spec No:41S–8.
6. Nishimura F, Murayama Y. Periodontal inflammation and insulin resistance-lessons from obesity. J Dent Res. 2001;80(8):1690–4.
7. Iacopino AM. Periodontitis and diabetes interrelationships: role of inflammation. Ann Periodontol. 2001;6(1):125–37.
8. Armitage GC. Development of a classification system for periodontal diseases and conditions. Ann Periodontol. 1999;4(1):1–6.
9. Promsudthi A, Pimapansri S, Deerochanawong C, Kanchanavasita W. The effect of periodontal therapy on uncontrolled type 2 diabetes mellitus in older subjects. Oral Dis. 2005;11(5):293–8.
10. Silness J, Loe H. Periodontal disease in pregnancy (II). Correlation between oral hygiene and periodontal condition. Acta Odontol Scand. 1964;22:121–35.
11. Loe H, Silness J. Periodontal disease in pregnancy (I). Prevalence and severity. Acta Odontol Scand. 1963;21:533–51.
12. Shlossman M, Knowler WC, Pettit DJ, Genco RJ. Type 2 diabetes mellitus and periodontal disease. J Am Dent Assoc. 1990;121(4):532–6.
13. Grossi SG, Skrepcinski FB, Decaro T, Robertson DC, Ho AW, Dunford RG, et al. Treatment of periodontal disease in diabetes reduces glycated haemoglobin. J Periodontol. 1997;68(8):713–9.
14. Kiran M, Arpak N, Unsal E, Erdogan MF. The effect of improved periodontal health on metabolic control in type 2 diabetes mellitus. J Clin Periodontol. 2005;32(3):266–72.
15. Iwamoto Y, Nishimura F, Nakagawa M, Sugimoto H, Shikata K, Makino H, et al. The effect of antimicrobial periodontal treatment on circulating tumor necrosis factor-alpha and glycated hemoglobin level in patients with type 2 diabetes. J Periodontol. 2001;72(6): 774–8.
16. Rodrigues DC, Taba MJ, Novaes AB, Souza SL, Grisi MF. Effect of non surgical periodontal therapy on glycemic control in patients with type 2 diabetes mellitus. J Periodontol. 2003;74(9):1361–7.
17. Dag A, Fırat ET, Arıkan S, Kadiroglu AK, Kaplan A. The effect of periodontal therapy on serum TNF-α and HbA1c levels in type 2 diabetic patients. Aust Dent J. 2009;54(1):17–22.
18. Christgau M, Palitzsch KD, Schmalz G, Kreiner U, Frenzel S. Healing response to nonsurgical periodontal therapy in patients with diabetes mellitus: clinical, microbiological and immunologic results. J Clin Periodontol. 1998;25(2):112–24.
19. Westfelt E, Rylander H, Blohme G, Jonasson P, Lindhe J. The effect of periodontal therapy in diabetics. Results after 5 years. J Clin Periodontol. 1996;23(2):92–100.
20. O'Connell PA, Taba M, Nomizo A, Foss Freitas MC, Suaid FA, Uyemura SA, et al. Effects of periodontal therapy on Glycemic control and inflammatory markers. J Periodontol. 2008;79(5):774–83.
21. Lim LP, Tay FB, Sum CF, Thai AC. Relationship between markers of metabolic control and inflammation on severity of periodontal disease in patients with diabetes mellitus. J Clin Periodontol. 2007;34(2):118–23.
22. Talbert J, Elter J, Jared HL, Offenbacher S, Southerland J, Wilder RS. The effect of periodontal therapy on TNF-α, IL-6 and metabolic control in type 2 diabetics. J Dent Hyg. 2006;80(2):1–16.
23. Mealey BL. Periodontal disease and diabetes: a two- way street. J Am Dent Assoc. 2006;137(Suppl):26S–31.
24. Yang PS, Wang Y, Oi XM, Ren JM, Ge SH. The effect of initial periodontal therapy on circulating TNF-α and HbA1c in type 2 diabetes patients with periodontitis. Zhongua Kou Qiang Yi Xue Za Zhi. 2003;38(5):364–6.
25. Iwamoto Y, Nishimura F, Soga Y, Takeuchi K, Kurihara M, Takashiba S, et al. Antimicrobial periodontal treatment decreases serum C-reactive protein, tumor necrosis factor-alpha, but not adiponectin levels in patients with chronic periodontitis. J Periodontol. 2003;74(8):1231–6.
26. Kardeşler L, Buduneli N, Cetinkalp S, Kinane DF. Adipokines and inflammatory mediators after initial periodontal treatment in patients with type 2 diabetes and chronic periodontitis. J Periodontol. 2010;81(1):24–33.
27. Yamazaki K, Honda T, Oda T, Ueki-Maruyama K, Nakajima T, Yoshie H, et al. Effect of periodontal therapy on the C-reactive protein and proinflammatory cytokine levels in Japanese periodontitis patients. J Periodontal Res. 2005;40(1):53–8.
28. Engebretson S, Chertog R, Nichols A, Hey-Hadavi J, Celenti R, Grbic J. Plasma levels of tumour necrosis factor-a in patients with chronic periodontitis and type 2 diabetes. J Clin Periodontol. 2007;34(1):18–24.
29. Bretz WA, Weyant RJ, Corby PM, Ren D, Weissfeld L, Kritchevsky SB, et al. Systemic inflammatory markers, periodontal diseases, and periodontal infections in an elderly population. J Am Geriatr Soc. 2005;53(9):1532–7.