The Effect of Non-Surgical Periodontal Therapy on Glycosylated Hemoglobin HBA1$_C$ Levels for Type II Diabetes Mellitus in Libyan Patients: Retrospective Interventional Study

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Abstract: <u>*Background*</u>*: The control of hyperglycemic levels in Diabetic patients reduces the risk of minor and major complications. It has been documented sever chronic periodontitis affects the glycemic control in patients with Diabetes. It has been reported by several clinical trials that treating chronic periodontitis in type II diabetic patients with phase I periodontal therapy reduces the levels of glycosylated hemoglobin of HBA1c by 0.4%.* <u>*Aim:*</u> *The aim of the present study is to observe the effect of non-surgical periodontal therapy on glycosylated hemoglobin levels in type II diabetic patients presented with chronic periodontitis.* <u>*Results:*</u> *Patients included in the study were recruited from Al Motamyaz private dental clinic. Forty-six patients with type II diabetes mellitus were included with different levels of severity for chronic periodontitis whom fit the inclusion criteria. All patients were treated by non-surgical debridement without the use adjunctive antibiotics. Full periodontal charting and HBA1c levels were recorded at baseline and three months after periodontal treatment. All clinical parameters including plaque score, bleeding score, and periodontal probing depths showed significant reduction at three months after non-surgical treatment with P value <0.001.HBA1c levels decreased significantly by 0.4% with P value =0.008.* <u>*Conclusion:*</u> *Chronic periodontitis and diabetes have a bidirectional relationship. The following study demonstrated that periodontal non-surgical treatment significantly reduces blood glucose levels after three months of reevaluation. A longer time of follow up is needed to evaluated the long-term effect of periodontal therapy on glycemic control for diabetic patients.*

Keywords: Diabetes mellitus, chronic periodontitis, glycosylated hemoglobin levels, periodontal phase I therapy, debridement

1. Introduction

There is a strong association between progression of periodontal disease and poor glycemic control in diabetic patients[1,2] which the latter is accurately measured by glycated hemoglobin levels (HBA1c)[3].It has been postulated that the chronic inflammatory state to subgingival bacteria in chronic periodontitis could affect the glucose tolerance which may negatively disturb the metabolic control especially in type 2 diabetes[4]. In a recent review, it was further confirmed that the pathogenic state of periodontitis which entails high inflammatory host response results in an increase insulin resistance[5].Which proves the existence of "two- way" relationship between the two chronic diseases [6.]

It has been suggested that severe chronic periodontal disease when diagnosed at baseline for diabetic patient has been associated with raised levels of HBA1c[7]. A systemic review by Lalla & Papapanou[8] showed that more periodontal destruction is present in form of severe clinical attachment loss, deep pockets and more teeth mobility in patients with poor glycemic control[8,9]. As it is well known from the classical literature that such changes in the periodontal tissue is due to the formation and binding of the glycation end products to the endothelial and blood cells resulting in the increase of apoptosis and delayed immune responses, leading eventually to delayed wound healing increase liability to infection[10,11].

However, it has been documented that periodontal treatment with or without antibiotics improves the glycemic control in diabetic patient[4]. In the same meta-analysis, interventional studies which were included, showed that the periodontal treatment that was offered to the type 2 diabetic patients (which consisted of non-surgical debridement (including supra and subgingival scaling and root planning) and the use of chlorhexidine or low doses of tetracycline or amoxicillin) patients had a significant decrease within the HBA1c levels by (- 0.4%)[4]. In a recent clinical trial, glycosylated hemoglobin was investigated before and 12 weeks after providing non-surgical periodontal therapy, showed a significant decrease in HBA1c (P -value 0.001)[12].

The aim of the following study is to see the effect of non-surgical periodontal therapy on glycemic control in type 2 diabetes mellitus patients by observing the changes in HBA1c levels at baseline and 3 months after treatment.

2. Materials and Methods

Patients included in the study were recruited from the Al Motamyaz private dental clinic. Patients record included those who have been seen in the clinic from April 2015 to May 2017. Verbal and written consent was gained. All patients which had type II diabetes mellitus were included. Patients were regularly seen by an endocrine consultant in terms of diet control and adjustment of medication doses. Patients included were either on Insulin injections or oral hypoglycemic drugs.The participants were 18 males and 28 females, with age range of 30 -72. Periodontally, all patients included had chronic periodontitis.

Inclusion criteria
- Patients diagnosed with type II diabetes mellitus.
- Medically free from any autoimmune disease
- Age above 20.
- Did not receive any kind of periodontal treatment in the past three months.

Exclusion criteria
- Medically diagnosed as type I diabetes mellitus.
- Took antibiotics in the past six months.
- Smoker more than 10 cigarettes a day.

Full medical history was taken for each patient and the levels of HBA1c was requested prior to the initiation of phase I therapy. Patients were asked to measure the HBA1c in the same laboratory to reduce level of error. Patients included their blood tests at these two laboratories (Al -Haya and Al Salem laboratories, Benghazi, Libya). Most of the patients took medication such as insulin injections, or oral hypoglycemic drugs and Metformin (Glucophage) according to their endocrine consultant. Three patients were advised on oral hypoglycemic drugs but refused medication and control their condition entirely by diet control. Panoramic radiographs and intra-oral peri-apical radiographs for selected teeth were done for all participants. Intra-oral examination done for all patients included full oral screening for any hard or soft tissue lesions. Full periodontal chartingdone using Michigan O' Probe with Williams calibration to record the clinical attachment loss and pocket probing depth along with plaque score, and bleeding score using O' Leary index[13].

Non-surgical periodontal therapy was conducted for all patients, which included giving oral hygiene instruction, patients were asked to use modified Bass technique, and interdental aids according to patient's needs. And the use of chlorohexidine mouthwash 0.12% concentration for a 2 weeks period during treatment. Full mouth debridement, supragingival, subgingival, and root debridement were provided over a period of two weeks provided by periodontist (L.A).

Patients were re-called every 2-4 weeks for reinforcing oral hygiene. After three months, full mouth periodontal charting was re-evaluated and patients were requested to re-do the HBA1c prior to the re-evaluation appointment. At three months Periodontal probing depth, plaque score and bleeding scores were measured in a similar way done in baseline. Statistical analysis was done using IBM SPSS statistical package. kolmogorov-smirnov test was used to compare the effect of non-surgical treatment on clinical parameters (Plaque score, bleeding score, periodontal probing depth) and HBA1c before and after treatment. And using general linear model ANCOVA to measure the significant relationship between different clinical parameters and HBA1c.

3. Results

a) Descriptive data
A total of 46 patients had type 2 diabetes mellitus were included by fitting the inclusion criteria. Mean age was 54.2

years. Age ranged from 34 to 75 years. As illustrated by the pie chart in (figure 2) 18 males and 28 females participated in the study.
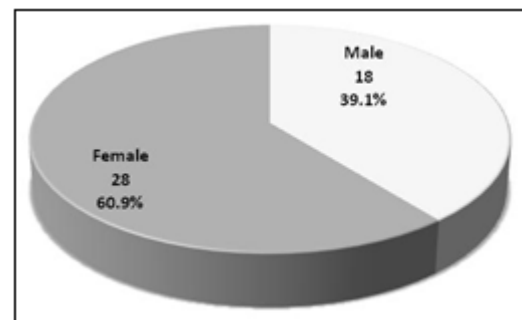

Figure 1: Number of male and female participants

In terms of diabetes control about 65.2% of the participants-controlled diabetes by insulin and oral hypoglycemic drugs, and only 10.9% controlled by diet(Figure 3).
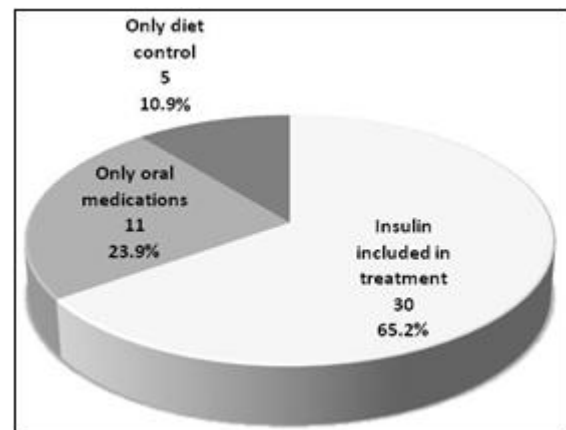

Figure 2: Diabetes mellitus control

Chronic periodontitis was diagnosed by full periodontal charting for patients. And periodontitis classified as mild, moderate or severe chronic periodontitis depending on the clinical attachment loss (CAL). This study had 45.7% of the patients diagnosed with severechronic periodontitis with CAL which was more than 5mm, whereas, 39.1% showed moderate chronic periodontitis with CAL range of 3-4mm, and 15.2% showed mild chronic periodontitis with CAL between 1 and 2mm. (figure 4).
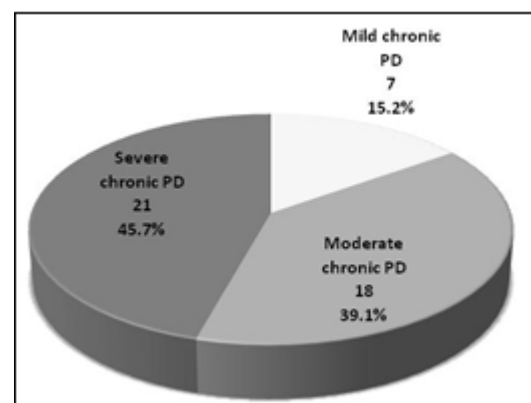

Figure 3: Classification of periodontal disease

b) General Inter-group variables, changes in clinical parameters

Plaque and bleeding scores
Changes in mean plaque score for all participants was investigated using t-test as this data group showed normal distribution. At baseline the mean plaque score was 73.22% reduced to a mean of 31.11% after treatment. Changes before and after treatment were significant with P value<0.001, as demonstrated by (figure 5).
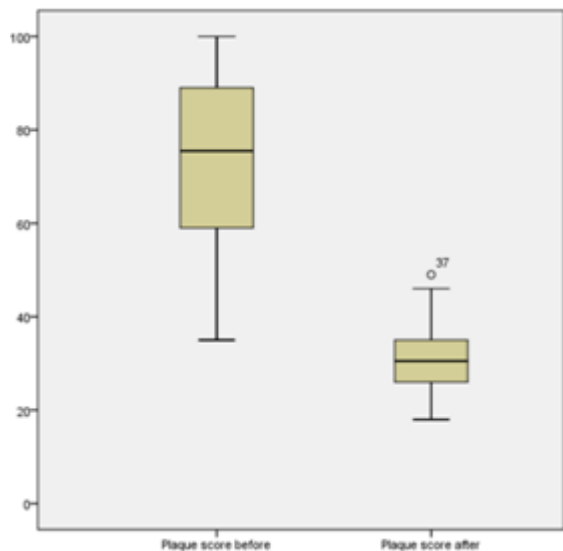

Figure 4: Changes in plaque score

Upper limit median bleeding score was 74.50 % at baseline reduced to 19.00 % after treatment. The median change in bleeding score using Wilcox test showed significant change before and after treatment, *P*<0.001. (Figure 6).
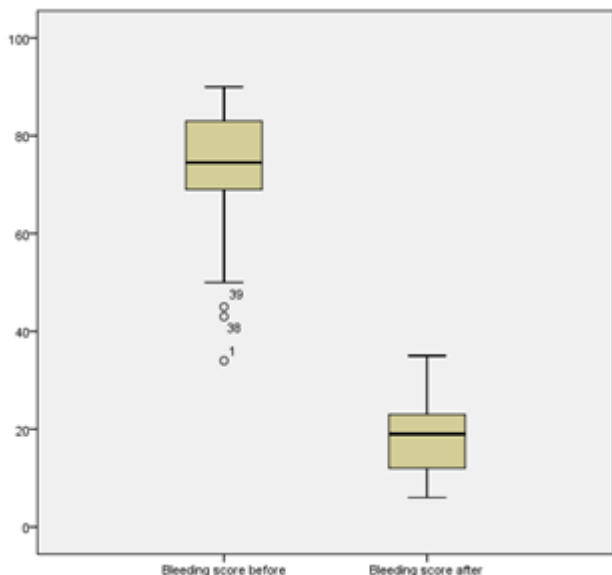

Figure 5: Difference in bleeding score before and after treatment

Periodontal pocket depth (PPD)
Most patients showed reduction in periodontal pocket depth after treatment, PPD before treatment was 6mm reduced to 4mm after treatment, which was statistically significant (*P*<0.001) (Figure 7).
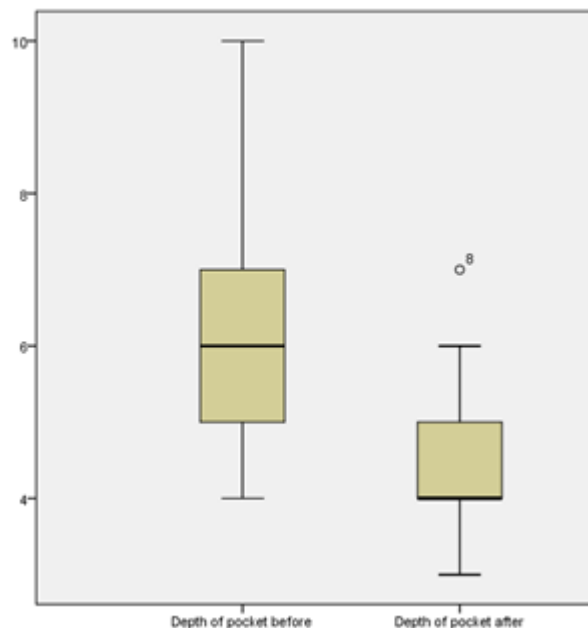

Figure 6: Changes in periodontal pocket depth before and after treatment

c) General Inter-group variables, changes in glycated hemoglobin levels (HbA1c) before and after treatment
The median difference in levels of HbA1c before (7.150%) and after treatment (7.000%) was approximately 0.4% which was statistically significant (*P* =0.008).
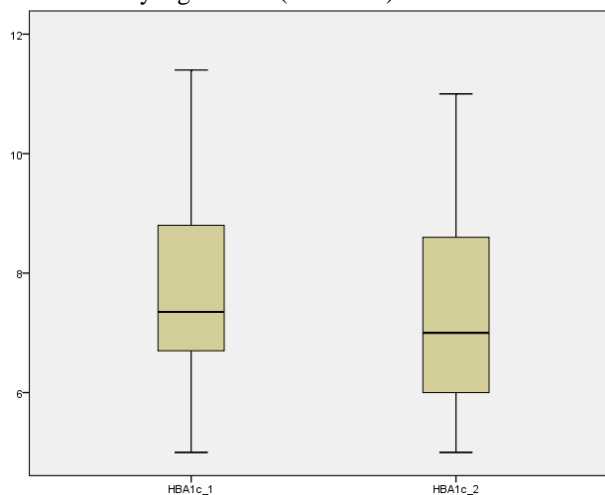

Figure 7: HbA1c levels before and after treatment

d) Analysis of repeated measures using multivariate models
Using general linear model ANCOVA revealed a significant relation between changes in level of plaque score before and after phase I therapy, with periodontal disease severity with a P- value 0.007. (Figure 9).
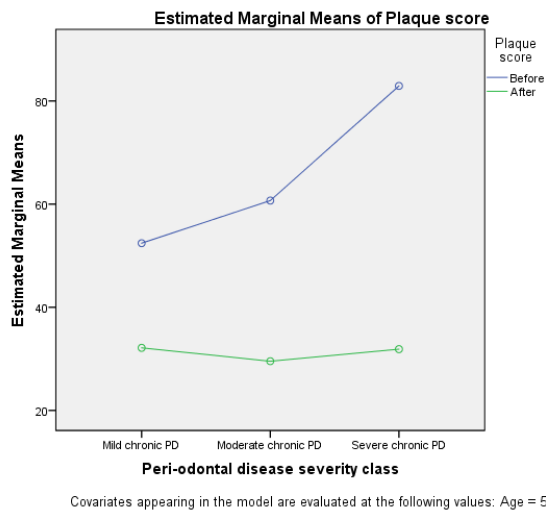
Figure 8: Relation of plaque score reduction according to PD severity

Bleeding score changes after treatment showed a marginal significant relation with periodontal severity with P- value 0.097.
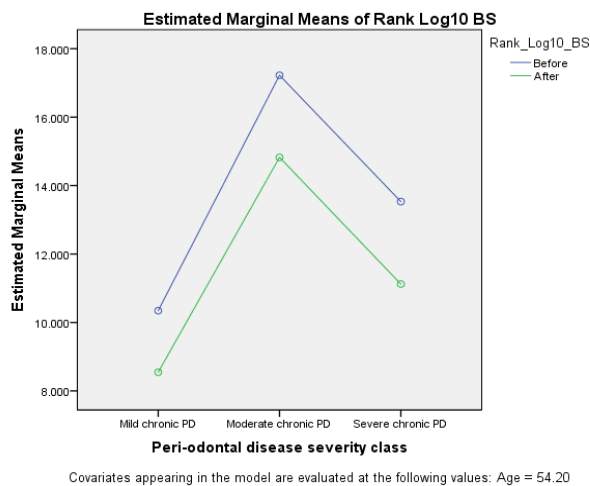

Figure 9: Model for bleeding score relation with periodontal disease severity.

Changes in Probing pocket depth before and after treatment also showed reduction in accordance with periodontal disease severity which is statistically insignificant with a P-value (0.955). (Figure 11).
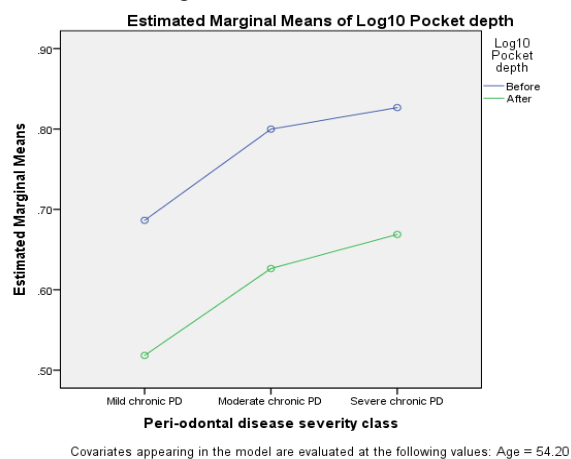

Figure 10: Linear model for relationship between PPD and PD severity

As for the HBA1c levels changes showed a relationship with periodontal disease severity which showed amarginal significance with a P-valueof (0.04). (Figure 12)
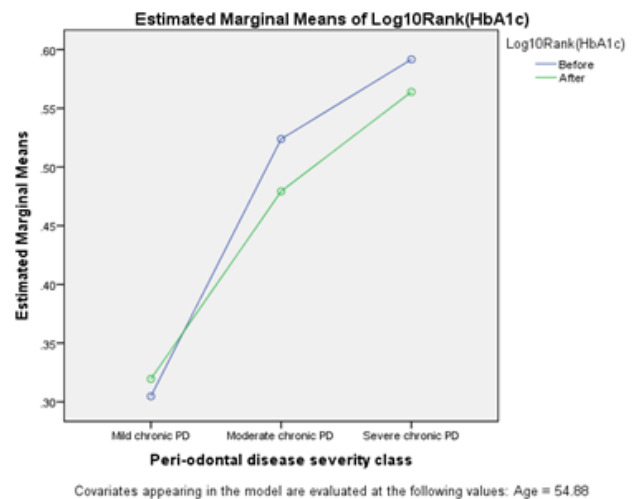

Figure 11: Relationship between reduction in HBA1c according to PD severity

4. Discussion

Periodontal disease has multiple local and systemic risk factors, one of these systemic factors is Diabetes mellitus (DM)[14-16]. It has been proved that periodontitis is the sixth complications for Diabetes mellitus [14,17,18].Diabetes mellitus control is investigated by the level of glycosylated hemoglobin by the blood test of HbA_{1C}. Which is recommended to be within the range from 6% to 7% [18].

The link between periodontitis and type II DM could be attributed to the formation of an irreversible protein known as Advanced glycation end products (AGEs) [5]. These products were found to attach to receptors known as RAGE [10] .The interaction presented between the AGEs and its receptors RAGE which is present in most body cells is one of the main reasons which give rise to the complications presented with DM[19].Other factors that may contribute to the complications associated with DM is the rise in the level of inflammatory cytokines [5] . It has been reported that patient with poor glycemic control and chronic periodontitis show high levels of IL-1β indicating which may contribute to the pathogenesis of periodontal disease in such patients [20, 21] .

Multiple clinical studies proposed that the high glucose levels presented in gingival crevicular fluid in patients with type II DM favors the growth of periodontal microbiota leading to the development of periodontitis [5] .It has been stated that the entry of periodontal pathogens and its virulence factors evokes systemic inflammation which may explain the link between the two chronic diseases[2].Multiple clinical trials have reported that non-diabetic and diabetic individuals with poor glycemic control demonstrated by the high levels of HBA1c have increased risk of periodontitis, and vice versa that patients with severe periodontitis have a risk of the diabetes onset [2, 5, 21].

Therefore, it has been recommended in a large Cochrane review that the treatment of chronic periodontitis and the

resolution of the inflammation helped in the reduction of HBA1c levels by approximately 0.5% [22, 23].

It is well reported by the literature that diabetic patients are twice to three times liable of developing chronic periodontitis [24], and this has been demonstrated by this study as 45.7% of the study sample suffered from severe chronic periodontitis. Whereas, 15.2% was diagnosed with mild chronic periodontitis.

After providing phase I therapy which includedoral hygiene instruction, supragingival and sub-gingival scaling with root debridement, all clinical parameters plaque, bleeding score, and probing depth showed reduction before and after treatment which all reached statistical significance ($P<0.001$). This is a similar to a recent clinical trial which presented that intervention treatment in 60 diabetic type II DM patients showed reduction in all clinical parameters and significant reduction in the levels of HBA1c [25].

As for glycemic control, diabetic patients included in the study showed 0.4% reduction in levels of HBA1c before and after treatment provided over the period of 3 months, which reached clinical significance with p-value of ($P =0.008$).In two systemic reviews, of multiple clinical trials which included a total of 371 patients with type II diabetic patients showed improvement in their glycemic control with a percentage of 0.5% over the period of 3 to 9 months [26,27].

Furthermore, the reduction in bleeding and plaque score after phase I therapy showed a significant relationship with periodontal severity with P value of 0.007 and 0.097 respectively. These results are similar to many previous clinical trials which show the great improvements in most clinical parameters after mechanical debridement for diabetic and non-diabetic patients[28].

The levels of HBA1c showed a relationship with periodontal disease severity, as its levels increases with severe chronic periodontitis when compared to moderate periodontitis as shown in figure 12. This is in agreement with EFP/AAP consensus report in regard the relationship of periodontal disease and systemic diseases [3].

5. Conclusion and Recommendations

The present clinical trial shows an improvement in the glycemic control of type II diabetic patients, after receiving a through phase I periodontal treatment over the period of 3months. Future recommendation would be to increase the sample size and evaluate patients for a long term follow-up.

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