

Original article

## Effect of Nonsurgical Periodontal Therapy On IL-36 Levels in Serum, Gingival Crevicular Fluid of Type 2 Diabetic and Non-Diabetic Patients with Chronic Periodontitis

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### ABSTRACT

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**Objective:** The aim of this study was to compare the level of inflammatory marker IL-36 $\beta$  in serum and gingival crevicular fluid in type 2 diabetic and non-diabetic patients with chronic periodontitis, before and after phase I therapy. **Methods:** A total of fifty subjects was included in this study; 20 Type 2 diabetic subjects with chronic periodontitis (group I) and 20 systemically healthy subjects with chronic periodontitis (group II) in addition to 10 systemically healthy subjects with clinically healthy gingiva as a control group (group III). The nonsurgical periodontal therapy was done to both group I and group II. Periodontal parameters, including plaque index, gingival index, bleeding on probing, probing depth and the clinical attachment level, in all the sites were recorded. GCF and serum were collected from all individuals included in the study; the first sample was collected from all groups (study and control) before phase I therapy. The second sample was collected 6 weeks after phase I therapy from group I & group II. Levels of IL-36 $\beta$  in GCF and serum were quantified using ELISA. **Results.** The current results showed statistically significant reduction in total level of IL-36 $\beta$  in serum and GCF in both groups; Type 2 diabetes with chronic periodontitis group (I) and systemically healthy with periodontitis group (II) after phase I therapy. Results also showed all clinical parameters were significantly improved after the phase I periodontal therapy in both groups I & II ( $p < 0.001$ ). **Conclusions.** Scaling and root planning (SRP) is the mainstay of treatment of periodontal diseases as SRP was effective in improving clinical parameters in diabetic and non-diabetic patients with chronic periodontitis. IL-36 $\beta$  could be used as a potential diagnostic marker for periodontal disease activity in both serum and gingival crevicular fluid.

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**Keywords:** IL-36 $\beta$ , Gingival Crevicular Fluid, Diabetes, Periodontitis.

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## INTRODUCTION

Periodontal disease is an inflammatory disorder in which tissue damage occurs through complex interactions between periodontal pathogens and components of the host mechanisms [1]. Many researchers assert that periodontal disease is the sixth complication of DM [2].

Interleukin-1beta (IL-1 $\beta$ ) and interleukin-6(IL-6) are two pro-inflammatory cytokines that play a major role in periodontal destruction [3]. The IL-36 subfamily is closely related to the IL-1subfamily because similar to the IL-1 $\alpha$  and IL-1 $\beta$  and IL-33, the IL-36Ra [4].

## METHODS

### *Subjects*

Fifty subject was selected for this study, their age ranges from 35-45 years, Group I:20 type 2 diabetic subjects with chronic periodontitis Group II: 20 systemically healthy subjects with chronic periodontitis Group III (control group): 10 systemic healthy persons with clinically healthy gingival. The selected patients were free from any systemic disease other than type 2 diabetes, and receiving no medication for the present condition three months prior to the study. Furthering, none of them had previous periodontal treatment, including scaling, root planning, and periodontal surgery in the last six months.

On other hand, smokers, alcoholic and pregnant and lactating patients were excluded from the present study. Clinical measurements: The full-mouth clinical periodontal parameters were recorded except the 3rd molars at baseline in all groups, and at 6 weeks after phase I therapy in group I and group II. periodontal status will be assessed by measuring specific indices such as: Plaque index. Gingival index. Bleeding on probing index. probing depth and Clinical attachment level.

### *Collection of gingival crevicular fluid (GCF) sample*

GCF samples were collected 2 times at the first appointment before scaling and root planning, and after 6 weeks in both group I and group II according to the following method: All clinically detected supra

gingival plaque was then removed carefully by sterile curettes and the surfaces were air-dried and isolated by cotton rolls. The sample was collected using commercially available periopaper. Paper strips were inserted into a crevice until mild resistance was felt, and left for 30 seconds, strips visually contaminated with blood and saliva were discarded. The paper was an immediate place after sample collection in the Eppendorf tube and stored at -700C. Paper points for each participant were pooled, and the GCF was extracted and assayed for the level of interleukin-36 $\beta$ . Serum sample: Two millimeters of blood were obtained from the cubital vein of each subject, at baseline and after 6 weeks of treatment in both of group I and group II. The whole blood samples were analysis in laboratory centrifuged at 3000 rpm for 15 min. The serum was separated carefully. Separated serum samples were collected in Eppendorf tubes and immediately transported to -20°C for freezing and storage. At baseline, blood samples were obtained from patients with type 2 diabetes were analyzed for HbA1c.

### *Statistical analysis*

Data were entered and statistically analyzed using the Statistical Package for Social Sciences (SPSS) version.

## RESULTS

Table 1 showed the demographic characteristics and baseline data of the patients enrolled in the study.

A total of fifty subjects was included in the study, with an age range from 35-45 years. They were divided into three groups: 20 subjects with T2DM with chronic periodontitis, and 20 subjects systemically healthy with chronic periodontitis and 10 subjects' systemic healthy persons with clinically healthy gingiva. The sample was composed of 28 female and 22 male. HbA1c (%) for T2DM 7.82 $\pm$ 1.96.

Variables	Patients with diabetes (n=20)	Patients without diabetes (n=20)	Controls (n=10)
Age (years) mean $\pm$ S	42.5 $\pm$ 3.	41.3 $\pm$ 3.2	40.2 $\pm$ 1.8
Age range (year)	(36-46)	(36-45)	(37-43)
Gender (M/F)	Male 8(40%) Female 12(60%)	Male 9(45%) Female 11(55%)	Male 5(50%) Female 5(50%)
HbA1c (%), mean $\pm$ SD	7.82 $\pm$ 1.96	-	-
Duration (year)	7.3750 $\pm$ 2.1 (4-12)	-	-

Table 2 presents the average of periodontal clinical parameters of patients in each group. PI, GI, BOP clinical parameters that no significantly different between the group I and II at baseline and after phase I therapy ( $p \geq 0.05$ ). But PD, CAL severity and extent showed significant difference between the group I and II at baseline, and after six weeks of phase I therapy ( $p \leq 0.05$ ).

**Table 2 clinical periodontal parameters (mean  $\pm$  SD) of study groups**

Periodontal clinical parameters	Group I T2DP(n=20)		Group II P(n=20)		Group III C(n=10)
	Baseline (M $\pm$ SD)	After phase I therapy (M $\pm$ SD)	Baseline (M $\pm$ SD)	After phase I therapy (M $\pm$ SD)	Baseline (M $\pm$ SD)
<b>Plaque index</b>	2.32 $\pm$ 0.35 <sup>*</sup>	0.45 $\pm$ 0.10 <sup>*</sup>	2.22 $\pm$ 0.35 <sup>*</sup>	0.38 $\pm$ 0.08 <sup>*</sup>	0.21 $\pm$ 0.04 <sup>@</sup>
<b>Gingival index</b>	2.28 $\pm$ 0.32 <sup>*</sup>	0.71 $\pm$ 0.13 <sup>*</sup>	2.14 $\pm$ 0.33 <sup>*</sup>	0.56 $\pm$ 0.08 <sup>*</sup>	0.25 $\pm$ 0.09 <sup>@</sup>
<b>Bleeding on probing</b>	89 $\pm$ 0.09 <sup>*</sup>	28 $\pm$ 0.07 <sup>*</sup>	85 $\pm$ 0.07 <sup>*</sup>	23 $\pm$ 0.06 <sup>*</sup>	17 $\pm$ 0.04 <sup>@</sup>
<b>Probing depth (mm)</b>	3.56 $\pm$ 0.58 <sup>no</sup>	2.52 $\pm$ 0.56 <sup>##</sup>	3.1 $\pm$ 0.50 <sup>no</sup>	2.09 $\pm$ 0.48 <sup>#</sup>	2.50 $\pm$ 0.54 <sup>@</sup>
<b>Clinical attachment Level (mm) Severity Extent</b>	3.74 $\pm$ 0.81 <sup>no</sup> 88.4 $\pm$ 8.8 <sup>no</sup>	2.29 $\pm$ 0.52 <sup>##</sup> 59.8 $\pm$ 6.98 <sup>##</sup>	3.2 $\pm$ 0.83 <sup>o</sup> 83.6 $\pm$ 6.90 <sup>no</sup>	1.7 $\pm$ 0.38 <sup>#</sup> 53.1 $\pm$ 5.67 <sup>#</sup>	Zero <sup>@</sup>

Table 3 showed the mean value of interleukin IL- 36 $\beta$  level in serum and GCF (pg/ml) in study groups at baseline and after six weeks of phase I therapy compared to control group II. Group I (type2 diabetic with chronic moderate periodontitis) showed highly significant differences of (IL- 36 $\beta$ ) level in serum and GCF between baseline and after six weeks of phase I therapy ( $p \leq 0.001$ ). At baseline, there were highly significant differences of (IL- 36 $\beta$ ) level in serum and GCF in group I compared with those in the group II and group III (systemically healthy subjects with moderate periodontitis and systemic healthy persons with clinically healthy gingival) ( $p \leq 0.001$ ). In group II, there were highly significant differences of (IL- 36 $\beta$ ) level in serum and GCF between baseline and after six weeks of treatment ( $p \leq 0.001$ ). At baseline, there were highly significant differences of (IL- 36 $\beta$ ) level in serum and GCF in group II compared with those in the group III ( $p \leq 0.000$ ). Also, and after six weeks, there were significant differences of IL- 36 $\beta$  ( $p \leq 0.001$ ) between group II and group III.

**Table (3). Serum and GCF IL-36 $\beta$  level in study groups before and after phase I therapy.**

Interleukins pg/mL in serum & GCF	Group I: T2DP(n=20)		Group II P(n=20)		Group III C(n=10)
	Baseline	After phase I therapy	Baseline	After phase I therapy	Baseline
<b>IL-36<math>\beta</math> in serum</b>	78.4 $\pm$ 11.6 <sup>**</sup>	69.8 $\pm$ 10 <sup>*§</sup>	49.9 $\pm$ 5.5 <sup>**</sup>	40.13 $\pm$ 4.8 <sup>#§</sup>	30.5 $\pm$ 5.4 <sup>@</sup>
<b>IL-36<math>\beta</math> in GCF</b>	55.05 $\pm$ 10.4 <sup>**</sup>	45.5 $\pm$ 6.6 <sup>*§</sup>	41.3 $\pm$ 4.2 <sup>**</sup>	31.3 $\pm$ 5.1 <sup>#§</sup>	26.8 $\pm$ 4.9 <sup>@</sup>

## DISCUSSION

The clinical findings of this study are consistent other study in which the levels of PI, GI, BOP, PD and CAL index after phase I therapy were significantly decreased versus their levels at baseline in type 2

diabetes with periodontitis as observed by Kardesler et al [5], and systemically healthy with chronic periodontitis Tuter et al [6]. In our study showed that positive correlations between HbA1c and periodontal clinical parameters (PI, PPD, CAL extent and severity). This result was coincidental with the result reported by Longo et al [7]. The serum and GCF IL-36  $\beta$  levels, in this study were found to be significantly higher in group I and group II as compared to those in the healthy controls group III, at baseline interestingly. Nothing is known about the role and presence of the recently identified cytokines IL-36  $\beta$  in type 2 diabetic with periodontal diseases in serum and GCF. This study has demonstrated for the first time and further investigations are needed to look at what role IL-36  $\beta$  have on the markers of periodontitis and in insulin resistance in the population with type 2 diabetes. In this study found that where significant positive correlation between serum and GCF IL-36 $\beta$  level and clinical parameter. Thus, we concluded that IL-36 $\beta$  are likely to be involved in the pathogenesis of periodontitis

## CONCLUSIONS

In conclusion, the present study demonstrated for the first time the presence of IL-36 $\beta$  serum levels in diabetic and non-diabetic with chronic moderate periodontitis. High levels of IL-36- $\beta$  in the diabetic group in comparison to the non-diabetic group might suggest that periodontitis in the chronic form could be related to the increase in serum and GCF IL-36 $\beta$ .

### *Disclaimer*

The article has not been previously presented or published, and is not part of a thesis project.

### *Conflict of Interest*

There are no financial, personal, or professional conflicts of interest to declare.

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