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## Evaluation of Serum Interleukin-10 and Matrix Metalloproteinase-9 Levels as Predictors of Glycemic Alteration in Type 2 Diabetes Mellitus in Patients with Periodontitis

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### ABSTRACT

**Purpose:** The present study was conducted to evaluate serum interleukin-10 and MMP-9 levels as predictors of glycemic alteration in type 2 Diabetic patients with periodontitis. **Subjects and methods:** This study was conducted on thirty (30) patients that were divided into two groups: Group 1 fifteen (15) patients with type 2 diabetes and periodontitis; Group 2 fifteen (15) patients with type 2 diabetes and c periodontitis receiving adjunctive treatment Omega-3 and aspirin. Elisa kit was used to evaluate the concentration of serum Mmp-9 and IL-10. **Results:** There was a statistically significant difference between (Group 1) and (Group 2) in the serum level of Mmp-9 (P-value 0.028) (P-value 0.010) after 3m and 6m as well as the serum level of IL-10(P-value 0.020) (P-value 0.029). **Conclusion:** Serum IL-10 can be used as predictor of glycemic alteration in type 2 Diabetes Mellitus. Omega-3 can be used as adjunctive treatment in periodontal disease.

### INTRODUCTION

Periodontitis is an inflammatory disease linked with bacterial biofilms linked with tooth-supporting tissue destruction. Its properties are gingival bleeding, the loss of clinical attachment (CAL), formation of periodontal pocketing and bone destruction <sup>(1)</sup>. Periodontitis is influenced by multiple factors including systemic diseases, genetic factors such as type 2

### KEYWORDS

Periodontitis,  
Type 2 diabetes,  
Mmp-9, IL-10,  
Omega-3 and aspirin.

- A paper extracted from Doctor Thesis titled "Evaluation of Serum Interleukin-10 and Matrix Metalloproteinase-9 Levels as Predictors of Glycemic Alteration in Type 2 Diabetes Mellitus in Patients with Periodontitis"

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diabetes and behavioral factors as oral hygiene level and smoking. The disease and the treatment are determined by a key factor which is the host response; despite the importance of bacterial biofilm formation for disease initiation <sup>(2)</sup>.

In most individuals, the extent of tissue destruction is limited by the protective aspect of the host response <sup>(3)</sup>. Although, the lesion can progress to a chronic inflammation state if the host inflammatory response is not adequately managing the microbial challenge and the tissue destruction. Periodontitis and systemic conditions as type 2 diabetes are caused by excessive and uncontrolled inflammation<sup>(4)</sup>.

Regarding the classification of periodontitis, the grading of periodontitis is influenced by the glycemic control level. Therefore, diabetes is considered as one of the important factors that may cause periodontitis <sup>(1,5)</sup>. Periodontitis and diabetes are inflammatory diseases where inflammatory mediators are involved in common pathogenic mechanisms, which have been suggested as possible biomarkers of the disease <sup>(6)</sup>. In accordance with the scientific data there is an existence of a two-way relationship between periodontitis and diabetes. Periodontitis negatively affects the diabetic status and diabetes increases the risk for periodontitis <sup>(7)</sup>.

The formation of advanced glycation end products (AGEs) is caused by hyperglycemia <sup>(8)</sup>. Matrix metalloproteinase (MMP) induces the release of cytokines caused by (AGEs) leading to the pathogenesis of periodontitis <sup>(9)</sup>. Gelatin is the preferred substrate of MMP-9. All types of collagen are included in the destruction process during periodontitis <sup>(10)</sup>, in stimulated whole saliva, the level of MMP-9 (gelatinase B) is increased in inflamed periodontal sites<sup>(11,12)</sup>.

The host response has a role in connective tissue destruction and bone resorption although the bacterial biofilm has a major role in the disease pathogenesis. It has become clear that tissue destruction is caused by host derived enzymes and

mediators like matrix metalloproteinase, cytokines, and other inflammatory mediators like prostaglandin E2 (PGE2). The development of host modulatory therapies (HMTs) is due to this shift in paradigm of concentration on host response <sup>(13)</sup>.

Using omega-3 is interesting due to their anti-inflammatory effect <sup>(2)</sup>. The addition of aspirin is due to its significant ability to produce resolvins that are more stable <sup>(14)</sup>. Resolvins, lipoxins and protectins drive the biological resolution of inflammation <sup>(15)</sup>.

## MATERIALS AND METHODS

### Study design

This study was done on thirty patients divided into two groups, each group consists of fifteen patients selected from the outpatient clinic in Oral medicine, Periodontology and Diagnosis department, Al-Azhar University.

The Protocol of the study was clarified for each patient after that an inform consent was signed by each participant. Research ethic committee approval was obtained.

### Patient grouping

- Group 1 (T2DM patients with CPD + SRP).
- Group 2 (T2DM patients with CPD + SRP and Omega-3 + Aspirin).

### Clinical Evaluation

#### *Gingival index*

The sites were evaluated at four sites (buccal, lingual, mesial, and distal) using (GI) of (Loe and Silness, 1963) <sup>(16)</sup>. The degree of inflammation was scored.

#### *Probing Depth*

It was obtained by measuring the probing pocket per site using William periodontal probe with following graduation: [1,2,3,5,7,8,9 and

10 millimeters (mm)]. Probing depth is measured at six points (midbuccal, midlingual, mesiobuccal, distobuccal, mesiolingual and distolingual) around each tooth. Probing depths were recorded at 1, 3 and 6 months for each patient, the deepest measurement was recorded.

### Clinical attachment loss

It was measured from using William periodontal probe at six points ( midbuccal, mid lingual, mesio-buccal ,distobuccal, mesiolingual and distolingual) around each tooth and recorded at 1, 3 and 6 months for each patient, the deepest measurement was recorded.

### Biochemical evaluation

The level of:

- Serum Interleukin-10 (IL-10).
- Serum Matrix metalloproteinase-9 (MMP-9).
- Glycosylated hemoglobin (HbA1c).

### Collection of samples

The serum samples were analyzed for IL-10 and MMP-9 using (ELISA) and enzyme- linked immunosorbant assay kit.

All study parameters were taken from each individual at:

- Baseline (immediately after the periodontal treatment)
- Three months after periodontal treatment.
- 6 months after periodontal treatment.

## RESULTS

### Clinical evaluation results (table 1)

#### Gingival Index (GI)

There was no statistically significant difference between the two groups at baseline, 3m and 6m.

#### Pocket depth (PD)

At 3m there was a statistically significant difference between the two groups.

#### Clinical attachment Loss (CAL)

At 3m and 6m there was a statistically significant difference between the two groups.

#### Biochemical evaluation:

#### MMP concentration, IL-10 concentration and Glycosylated Hg

At 3m and 6m there was a statistically significant difference between the two groups.

**Table (1)** The mean, standard deviation (SD) values of Clinical parameters of different groups.

Variables			Group 1	Group 2	p- value
GI	Baseline	Mean	2.67	2.53	0.464ns
		SD	0.49	0.52	
	3m	Mean	2.2	1.93	0.213ns
		SD	0.56	0.59	
	6m	Mean	1.87	1.6	0.104ns
		SD	0.35	0.51	
	p-value		<0.001*	<0.001*	
PD	Baseline	Mean	6	5.93	0.826ns
		SD	0.85	0.8	
	3m	Mean	5.73	5	0.015*
		SD	0.7	0.85	
	6m	Mean	5	4.4	0.084ns
		SD	1	0.83	
	p-value		0.005*	<0.001*	
CAL	Baseline	Mean	6.47	5.8	0.109ns
		SD	0.74	1.37	
	3m	Mean	6.13	4.87	0.003*
		SD	0.74	1.3	
	6m	Mean	5.27	4.27	0.013*
		SD	0.8	1.22	
	p-value		0.003*	0.001*	

\* Significant  $p \leq 0.05$

## DISCUSSION

The results of the present study showed that all clinical parameters including in both groups have been improved at 3 and 6 months. The results of group 1 are in accordance to another study reported that periodontal therapy resulted in significant improvement in GI, PD and CAL 3 month after treatment <sup>(17)</sup>. Our results are also in accordance with a study that showed that SRP resulted in improvement in GI and PD 6-month post-treatment <sup>(18)</sup>. This improvement was due to nonsurgical periodontal therapy tended to reduce systemic inflammation and the concentration of circulatory cytokines <sup>(19)</sup>.

Group 2 taking a combination of omega 3 and aspirin yielded a more statistically significant improvement in clinical parameters than do group 1. The results of glycated hemoglobin (HbA1c) in group 1 showed a non-significant reduction in the level of HbA1c. While group 2 showed an improvement in the glycemic control. Group 2 had a more significant reduction in HbA1c than do group 1 after 3 and 6 months <sup>(18)</sup>. The improvements in our finding in group 2 could be attributed for omega-3 and aspirin in humans is known to increase circulating levels of resolvins which suggests a potential for therapeutic benefit.

The results of the study showed that serum level of IL-10 is increased non-significantly in group 1 and significantly in group 2, however this increase was more significant in group 2 in comparison to group 1 after 3 and 6 months, while MMP-9 level is decreased 6 months after treatment in both groups with the reduction being more significant in group 2 than group 1. Results of group 1 is not exactly in line with a study where effective periodontal therapy resulted in reduction in MMP-9 however this doesn't reach statistical significance which is not the case in our study <sup>(20)</sup>.

## CONCLUSION

- Serum IL-10 and MMP-9 can be used as predictor of glycemic alteration in type 2 Diabetes Mellitus.

- Omega-3 can be used as adjunctive treatment in periodontal disease.

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