Research Paper

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A comparative Study on Serum Leptin and Adiponectin levels in Periodontitis Patients with and without Diabetes Mellitus Type2

Microbiology

KEYWORDS : periodontitis, type 2 diabetes mellitus, leptin and adiponectin

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ABSTRACT

Background: Periodontal diseases are initiated by microbial plaque, which accumulates in the sulcular region and induces an inflammatory response. Recently studies found that periodontitis might be related to several systemic diseases especially diabetes mellitus. In recent years, there has been intense interest in the role of the adipose tissue derived substances that named adipokines in the inflammatory diseases of the human being including the inflammatory periodontitis. Aims of study: This study was performed to evaluate the serum level of leptin and adiponectin in periodontitis with and without type 2 diabetes mellitus (T2DM), to determine the association between serum level of the biochemical markers (leptin and adiponectin) with clinical periodontal parameter and determine the correlation between adiponectin and leptin levels. Material and Methods: Sixty patients (30 periodontitis patients and 30 periodontitis+T2DM patients) and 25 apparently healthy volunteers were enrolled in this study. Periodontal parameters used in this study were plaque index, gingival index, probing pocket depth, clinical attachment level and bleeding on probing. Serum levels of leptin and adiponectin were estimate by ELISA. Results: The present data revealed a significant elevation ($p<0.01$) in mean level of leptin in periodontitis group and periodontitis+T2DM group in comparison to that in healthy control, moreover, the comparison between two groups of patients showed that the mean level of leptin was increase in periodontitis+T2DM group but statistically not significant ($p>0.05$). On the other hand, there is significant decrease ($p<0.001$) in serum adiponectin in patients groups when compared to control group, additionally, there is slight significant reduction in mean level of adiponectin in periodontitis patients without DM when compared to those patients with DM, ($p<0.05$). Interestingly, negative significant correlation was noticed between leptin and adiponectin in periodontitis patients and periodontitis+T2DM group. Additionally, these findings did not observe any significant correlation between serum leptin, and adiponectin with clinical periodontal parameters ($p>0.05$). Conclusion: This study demonstrates that serum levels of leptin and adiponectin play a crucial role in pathogenesis of periodontitis with and without.

Introduction

Periodontal diseases are comprised of a group of inflammatory conditions that result in the destruction of the supporting structures of the dentition, leading to loss of the connective tissue attachment and alveolar bone, resulting in loss of the teeth. Though the microorganisms are implicated as the etiologic agent to bring about inflammatory lesion, the chemical mediators of inflammation play a pivotal role in the loss of connective tissue, as well as supporting alveolar bone (Carenza, 2009). Cytokines like interleukin- 1β, (TNF- α), prostaglandin-E2 and adipocytokines like adipopnectin and leptin has been shown to orchestrate the host response to infection and inflammatory stimuli (Gesta et al., 2007). However; evidences indicate that periodontitis may have profound effects on systemic health. Epidemiologic studies reported that greater prevalence or severity of periodontitis was seen in diabetic individuals than in non-diabetic subjects (Taylor and Borgnakke, 2008).

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycaemia due to the defective secretion or activity of insulin. DM present with the classical triad of symptoms such as polydypsia, polyuria and polyphagia. This is often accompanied by chronic fatigue and loss of weight. Complications of DM include retinopathy, nephropathy, neuropathy, and cardiovascular disease (Khader et al., 2008). Periodontitis is now referred to as the fifth most common complication of diabetes. Clinical studies have demonstrated a higher prevalence of periodontitis in diabetic patients. Periodontal disease and diabetes have a number of common pathways in their pathogenesis; both diseases are polygenic disorders with some degree of immunoregulatory dysfunction (Soskolne et al., 2001). With the start of the current century, there is increased in the interest about the role of the adipose tissue that produces and releases a variety of inflammatory factors, including adiponectin, resistin, leptin and visfatin, as well as cytokines such as TNF-α and IL-6. These factors and cytokines are thought to play a role in inflammation and immune responses (Lago et al., 2007). Adipokines are bioactive mediators released from the adipose tissue including adipocytes and other cells present within fat tissues. These include several novel and highly active molecules released abundantly by adipocytes like leptin, resistin, adiponectin and visfatin (Tilg and Moschen., 2006).

Adiponectin (ADP), a 30-kDa protein, mainly secreted by adipocytes, has anti-inflammatory, antidiabetic, and anti-atherogenic properties, which circulates in high concentrations in the blood. Adiponectin levels are decreased in individuals with obesity, DM type2 and cardiovascular disease. Adiponectin inhibits osteoclast formation stimulated by lipopolysaccharide (LPS) from Actinobacillus actinomycetemcomitans. Regulation of adiponectin is provided by inflammatory cytokines such as IL-6 and TNF-α (Yamaguchi et al., 2007). Leptin (LEP) is a 16-kDa nonglycosylated peptide hormone. It is synthesized mainly in adipocytes and in minor quantities by T cell, osteoblast and gastric epithelium. Leptin has been classified as a cytokine as it shows structural similarities to the IL-6 and IL-11 (Rosa et al., 2010). The overall increase in leptin during infection and inflammation indicates that leptin is a part of the immune response and host defense mechanisms. Since, leptin has a role in the inflammatory response. An increase in leptin level in healthy gingiva may be a host defense mechanism as during sepsis (Sanchez and Romero., 2001). Therefore, this study was performed to evaluate the serum level of leptin and adiponectin in periodontitis with and without T2DM, to determine the association between serum level of the biochemical markers (leptin and adiponectin) with clinical periodontal parameters, and to investigate the correlation between leptin and adiponectin.

Subjects and Methods

A total of 60 patients with periodontitis consist of (30 periodontitis patients and 30 periodontitis+T2DM patients) were studied, their ages range from 32-64 years with a mean age of (47.60±8.48 and 48.16±8.34 years, respectively). Apparently healthy volunteers consisted of 25 individuals who were their

age range (32-64) years with mean age of (44.76±8.29) years considered as control. Periodontal parameters used in this study were plaque index, gingival index, probing pocket depth, clinical attachment level and bleeding on probing. Blood samples were collected from all patients and controls, and then serum was separated from blood to estimate the levels of leptin and adiponectin by enzyme-linked immunosorbent assay.

Statistical analysis: It was assessed using P (T-test), P (ANOVA test). Correlation among different parameters was calculated by the Spearman correlation coefficient test, P value less than the 0.05 was considered statistically significant.

Results

The distribution of ages, sexes and BMI of patients groups and controls group included in this study are presented in table (1). No statistically significant differences (p>0.05) in age or gender existed among study groups. Furthermore, there was slight male's predominance among periodontitis group about (63.3%) of patients were males, while only (36.7%) were females, in periodontitis +T2DM group about (60%) of patients were males, and (40%) were females Regarding the mean of BMI, the current results found that there are no significant differences (p>0.05) in the mean of BMI among study groups, in periodontitis group the mean of BMI was 22.43±4.10 Kg/m2, in periodontitis +T2DM group the mean of BMI was 22.95±3.4 Kg/m2 and in control group the mean of BMI was 22.42±3.25 Kg/m2, as clearly shown in table (1).

Table -1: Distribution of ages, sexes and BMI in study groups.

Characteristics		Study groups			P-value
		Healthy control n=25	Periodontitis n=30	Periodontitis +T2DM n=30	
Age and Sex					
Age (years)	Range	(32-64)	(32-64)	(32-64)	
	Mean ± SD	44.76±8.29	47.60±8.48	48.16±8.34	0.43^{NS}
Gender type	Female	17 (68%)	11(36.7%)	12 (40%)	
	Male	8 (32%)	19 (63.6 %)	18 (60%)	0.672^{NS}
BMI (Kg/m2)					
BMI	Mean ± SD	22.42±3.25	22.43±4.10	22.95±3.4	0.665 ^{NS}

NS=Not significant (p>0.05).

The differences in clinical periodontal parameters in patients and healthy controls are summarized in table (2). This study is demonstrated that the mean value of PI, GI, PPD, CAL and BOP were significantly higher (P<0.001) in periodontitis group and periodontitis patients with T2DM when compared to controls group. On the other hand, there are no significant differences (p>0.05) in the mean value of all clinical periodontal parameters between two groups of periodontitis patients.

Table -2: Clinical Periodontal Parameters in Study Groups.

Clinical periodontal Parameters	Study groups			P-value
	Healthy control n=25	Periodontitis n=30	Periodontitis+T2DM n=30	
Plaque index	0.79±0.39	1.43±0.39	1.54±0.66	<0.001**
Gingival Index	0.74±0.28	1.30±0.46	1.29±0.45	<0.001**
Probing Pocket Depth (mm)	0.84±0.39	2.23±0.79	2.23±0.94	<0.001**
Clinical Attachment Loss (mm)	0.0	2.37±0.85	2.30±1.03	<0.001**
Bleeding on Probing (BOP)	5.76±1.67	25.34±26.61	24.66±9.79	<0.001**
Control X periodontitis<0.001** Control X periodontitis +T2DM<0.001** periodontitis X periodontitis +T2DM [NS]				

**** = Highly significant difference (p≤0.001).**

Table (3) revealed a significant elevation in mean serum level of leptin in periodontitis group (25.89±5.52 ng/ml) and in periodontitis+T2DM patients (32.16±7.78 ng/ml) as compared to healthy control (16.66±3.93 ng/ml), (p<0.01). Moreover, the comparison between two groups of patients showed that the mean level of leptin was increase in periodontitis+T2DM group but statistically not significantly (p>0.05). On the other hand this study observed that there is significant decrease (p<0.001) in mean serum level of adiponectin in periodontitis patients (60.08±9.61 ng/ml (and periodontitis+T2DM patients (50.10± 7.64 ng/ml) in comparison to that in healthy control (77.57±10.80 ng/ml). Additionally, there is slight significant reduction in mean serum level of adiponectin among periodontitis patients without T2DM when compared to those patients with T2DM, (p<0.05), according to table (4).

Table-3: The differences in mean serum levels of leptin (ng/ml) among study groups.

Serum Leptin	Control group n=25	Periodontitis n=30	Periodontitis+T2DM n=30	p-value
Range	(1.10-50.92)	(0.7-77.55)	(1.84-60.14)	
Median	11.0	23.93	22.82	
Mean	16.66	25.89	32.16	0<0.01*
S.D.	3.93	5.52	7.78	
Control X periodontitis0<0.01* Control X periodontitis +T2DM 0<0.01* Periodontitis X periodontitis +T2DM >0.05				

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Table -4: The differences in mean serum levels of adiponectin (ng/ml) among study groups.

Serum Adiponectin	Healthy control (25)	Periodontitis (30)	Periodontitis + T2DM (30)	p-value
Range	(17.72-94.44)	(19.24-94.36)	(21.05-98.44)	
Median	79.22	63.40	63.40	
Mean	77.57	60.08	50.10	0<0.001**
SD	10.80	9.61	7.64	
Control X periodontitis<0.001** Control X periodontitis+T2DM <0.001** Periodontitis X periodontitis+T2DM <0.05*				

The results of correlation between leptin and adiponectin are clearly shown in figures (1 and 2). An anticipated, leptin level was showed significant negative correlation with adiponectin in both groups of patients; in periodontitis group patients was (r=-0.325, p=0.011) and in periodontitis+T2DM group of patients was (r=-0.434, p=0.017). Meanwhile Spearman correlation coefficient test between (leptin and adiponectin) and clinical periodontal parameters (PI, GI, PPD, CAL and BOP) were shown in tables (5 and 6). The current study did not observe any significant correlation between serum level of both hormones and clinical periodontal parameters (p>0.05), however; there is weak positive non significant correlation between serum level of leptin and PPD (r=0.281; p= 0,083), table (5).

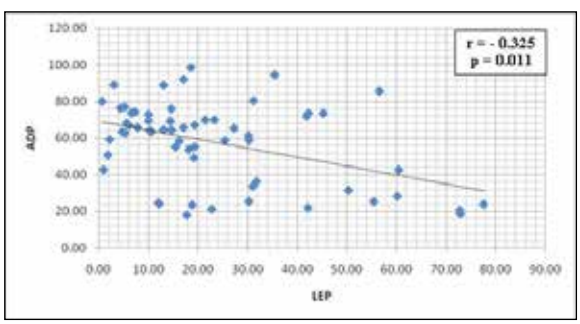

Figure-1: Correlation between leptin and adiponectin in periodontitis patients group

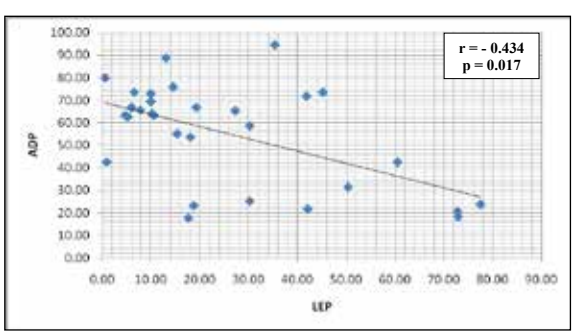

Figure-2: Correlation between leptin and adiponectin in periodontitis+T2DM patients group

Table-5: Correlation between leptin level and clinical periodontal parameters.

Leptin	R-value	P-value
PI	0.160	0.397
GI	-0.147	0.438
PPD	0.281	0.083
CAL	-0.083	0.663
BOP	-0.081	0.671

Table-6: Correlation between adiopnectin and and clinical periodontal parameters.

Adiponectin	R-value	P-value
PI	-0.133	0.482
GI	-0.224	0.093
PPD	0.008	0.965
CAL	0.090	0.636
BOP	-0.032	0.868

Discussion

In the present study a predominance of periodontatis among males than a female which is comparable with other Iraqi study conducted by Mohssen (2013), whereas, disagree with the result of (Ali et al., 2008) who observed that periodontitis in males less than as in females. The large prevalence of periodontitis among males may be due to that male less interest in oral hygiene than males. Also, current result was comparable with other local study performed by Karam (2013) who found that there were no significant differences in the mean of BMI between periodontitis patients and control group.

The present result was consistent with other result reported by Abaas (2006) and AL-saidy (1996), they found that there was significant increase in mean of periodontal parameter (PI, GI, PPD, CAL and BOP) in patients with T2DM compared to healthy control. Similarly (Karam, 2013) found that the mean value of each PI, GI, PPD, CAL and BOP were significantly higher in periodontitis patients when compared to healthy controls. Rodrigues et al.,(2003) indicated that diabetes can result in more severe periodontal destruction than in matched non-diabetes groups. Increase the risk for periodontitis is dependent on glycaemic control and the duration of diabetes.

These findings were similar to other finding reported by Karam (2013), who showed that the circulating level of leptin in serum was correlated positively with periodontitis diseases. Correspondingly, Karthikeyan and Pradeep in 2007 suggest that greater the periodontal destruction, the greater in the serum leptin concentration and the lowest serum leptin concentration was found in healthy individuals. In addition Matsubara et al., 2002 and Turki et al., 2012 observed a significant increased level of leptin in type 2 diabetic male patients. Moreover, Wu et al. (2000), who demonstrated that leptin levels in diabetics are higher than in normal subjects and that T2DM is associated with hyperinsulinaemia and insulin resistance compared to the control group.

Two explanations have been proposed for the increase of the serum levels of leptin in periodontitis: firstly, the gingival inflammation would result in vasodilatation, which would increase the serum levels of leptin. Secondly, the serum levels of leptin would increase as a defense mechanism of the body, to fight the periodontal inflammation (Bullon et al., 2009). Recently, Gundala et al in 2012 mentioned that elevated serum leptin concentration is associated with chronic periodontitis could be considered as one of the risk markers, and Duarte et al in 2012 found that serum level of leptin was significantly higher in periodontitis patients when compared to healthy controls suggesting that periodontitis upregulated the circulating level of leptin in subjects with normal BMI. In contrast to the present result Davies et al in 2011 pointed out to that the level of serum leptin was not significantly different between periodontitis patients and healthy subjects.

Regarding serum adiponectin this study showed decreased levels of serum adiponectin in periodontitis patients group and periodontitis+T2DM disease patients group when compared to healthy control. Prospective and longitudinal studies indicated that lower adiponectin levels were associated with a higher incidence of type 2 diabetes (Mather et al., 2008). Moreover, another study by Luo et al., 2010, demonstrated that lower adiponectin level associates with impaired gloucose tolerance and T2DM in Asian Indian women. On the other hand, the results reported by Furugen et al., (2008) were at variance with current

results, who indicated that there was no significant differences in adiponectin levels among patients with periodontitis in Japanese people when compared to healthy controls.

The present result concordant with another study done by Jing Ling et al., (2014), who showed that the level of serum leptin was increased in both groups of patients when compared to healthy group, while the level of serum adiponectin was decreased in patients groups as compared to the healthy group. Correspondingly, Chan-Hee et al., (2013), observed that there was inverse correlation between serum adiponectin and leptin in Korean patients with T2DM. Conversely, Putz and colleagues showed that there was no association was found between serum adiponectin and serum leptin levels in T2DM patients (Putz et al., 2004). The imbalance between adiponectin (anti-inflammatory) and leptin (pro-inflammatory) in periodontitis with T2DM diseases determine the degree of inflammation which can lead to major clinical effects.

Finally, results of present study are inconsistent with other results reported by (Karam, 2013; Jing Ling et al., 2014) who found that there was significant positive correlation between serum leptin levels and clinical periodontal parameters (PI, GI, PPD, CAL and BOP). Meanwhile Shimada et al., (2010) found that serum leptin level was associated with mean probing depth, mean clinical attachment level and mean alveolar bone loss in the study population. So they concluded that this may be due to differences in disease stage between patient or that leptin levels is correlated to the degree of inflammation present and with no association to the degree of periodontal destruction represented by CAL this seems to be the possible logical explanation. On the other hand, Jing Ling and associates found that the concentration of serum adiponectin was significantly negative correlated with periodontal parameters and the ratio of leptin/ adiponectin showed strong positive correlation with clinical periodontal parameters (Jing Ling et al., 2014). The discrepancies observed between various studies could be caused, in part, to the differences in the sample size of each study, differences in types of samples used for each study and differences in sampling methods. In conclusion, these finding demonstrates that serum levels of leptin and adiponectin play a crucial role in pathogenesis of periodontitis with and without T2DM.

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