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Evaluation of Serum Leptin and Adiponectin Levels in Iraqi Patients with Chronic Periodontitis

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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 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 Iraqi periodontitis patients, 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.*
Material and Methods: *Thirty patients with chronic periodontitis 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 adiponectinwere estimatedby ELISA.*
Results:*The present data revealed a significant elevation ($p<0.01$) in mean level of leptin in chronic periodontitis in comparison to that in healthy control.On the other hand, there is significant decrease ($p<0.001$) in serum adiponectin in patients groups when compared to control group,the ratio of leptin\adiponectin was significantly higher among periodontitis patient group when compared with the ratio in the control group, ($P<0.01$).Interestingly, negative significant correlation was noticed between leptin and adiponectinamongpatients. Additionally, these findings did not observeany significant correlation between serum leptin, adiponectin, and ratio of leptin/adiponectin with clinical periodontal parameters ($p>0.05$).*
Conclusion*: this study demonstrates that serum levels ofleptin and adiponectin play a crucial role in pathogenesis of periodontitis and the relative leptin/adiponectin ratio appears to be indicative of disease occurrence.*
Keywords:*periodontitis,leptin and adiponectin.*

I. 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 toinfection and inflammatory stimuli (Gestaet al., 2007).

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 tissueincluding 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 *Actinobacillusactinomycetemcomitans*. 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 chronic periodontitis..

II. Subjects And Methods

A total of 30 patients with chronic periodontitis were studied, their ages range from 32-64 years with a mean age of (47.60±8.48years).Apparently healthy volunteers consisted of 25 individuals who were their age range 32-64years with mean age of (44.76±8.29 years) considered as control. Periodontal parameters used in this study were plaque index (PI), gingival index (GI), probing pocket depth (PPD), clinical attachment level (CAL) and bleeding on probing (BOP). 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 immune sorbent assay.

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

III. Results And Discussion

The demographic characteristics 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 between two groups. Furthermore, there was slight male's peredominance among patients group about (63.3%) of patients were males, while only (36.7%) 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, as clearly shown in table (1).

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

Characteristics		Study groups		
		Healthy control n=25	**Periodontitis n=30**	**P-value**
Age and Sex				
Age (years)	Range	(32-64)	(32-64)	
	Mean ± SD	44.76±8.29	47.60±8.48	0.43^{NS}
Gender type	Female	17 (68%)	11(36.7%)	
	Male	8 (32%)	19 (63.6 %)	0.672^{NS}
BMI (Kg/m2)				
BMI	Mean ± SD	22.42±3.25	22.43±4.10	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 (1.43±0.39; 1.30±0.46; 2.23±0.79; 2.37±0.85 and 25.34±26.61) when compared to controls group (0.79±0.39; 0.74±0.28; 0.84±0.39; 0.0; 5.76±1.67), respectively.

The present result was consistent with other result reported by (Karam, 2013) who found that the mean value of each PI, GI, PPD, CAL and BOP were significantly higher in periodontitis patients when compared to healthy controls.

Although the bacterial biofilm is necessary for the development of the periodontal disease, it alone is not enough to produce the disease. The host response, through the releasing of a large spectrum of proinflammatory mediators, is responsible for great part of the periodontal tissue destruction observed in the disease (Andriankajaet al., 2010).

Table-2: Clinical Periodontal Parameters in Study Groups.

Clinical periodontal Parameters	Periodontitis n=30	Healthy control n=25	P-value
Plaque index	1.43±0.39	0.79±0.39	<0.001**
Gingival Index	1.30±0.46	0.74±0.28	<0.001**
Probing Pocket Depth (mm)	2.23±0.79	0.84±0.39	<0.001**
Clinical Attachment Loss (mm)	2.37±0.85	0.0	<0.001**
Bleeding on Probing (BOP)	25.34±26.61	5.76±1,67	<0.001**

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

Table (3) revealed a significant elevation in mean serum level of leptin in periodontitis patients (25.89±5.52) as compared to healthy control (16.66±3.93), (p<0.01). The result was similar to the study performed 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 who suggest that greater the periodontal destruction, the greater in the serum leptin concentration and the lowest serum leptin concentration was found in healthy individuals.

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 (Bullonet al.,2009).

Recently, Gundalaet al in 2012 mentioned that elevated serum leptin concentration is associated with chronic periodontitis could be considered as one of the risk markers, and Duarteet al in 2012 found that serum level of leptin was significantly higher in periodontitis patients when compared to healthy controls suggesting that periodontitis up regulated the circulating level of leptin in subjects with normal BMI. In contrast to the present result Davieset al in 2011 pointed out to that the level of serum leptin was not significantly different between patients and control.

Table-3: The differences in mean serumlevels of leptinbetweencontrols and patients.

Serum Leptin	Control group n=25	Periodontitis n=30	p-value
Range	(1.10-50.92)	(0.7-77.55)	
Median	11.0	23.93	
Mean	16.66	25.89	**0<0.01***
S.D.	3.93	5.52	

The current study observed that there is significant decrease (p<0.001) in mean serum level of adiponectininin chronic periodontitis patients (60.08±9.61) in comparison to that in healthy control (77.57±10.80).Adiponectin enhances production of anti-inflammatory cytokines including IL-10 and the IL-1 receptor antagonist, part of the evidence for its anti-inflammatory role. Furthermore, adiponectin can indirectly decrease IL-6 and TNF-α. Because of its anti-inflammatory properties, adiponectin is important in metabolic disorders including obesity, type II diabetes, coronary heart disease, and metabolic syndrome (Odaet al., 2008).

The present results agreed with study performed by (Jing Ling et al., 2014), who indicated that decreased levels of serum adiponectin in patients with periodontitis when compared to healthy control.Pischonet at., 2007, indicated that adiponectinis a hormones secreted from the fat tissue, the levels of adiponectin are reduced in people with obesity, insulin resistance .On the other hand, the results reported by Furugenet al., (2008) were at variance with current results, who indicated that there were no significant differences in adiponectin levels among patients with periodontitis in Japanese people when compared to healthy controls.

Table -4: The differences in median serumlevels of adiponectin between controls and patients.

Serum Adiponectin	Healthy control (25)	Periodontitis (30)	p-value
Range	(17.72-94.44)	(19.24-94.36)	
Median	79.22	63.40	
Mean	77.57	60.08	0<0.001**
SD	10.80	9.61	

Determination the ratio of leptin\ adiponectin in current study revealed, that there was significant differences between patient group and controls group. The mean serum level of leptin\ adiponectin ratio in periodontitis group (0.43±0.08) are significantly higher (P<0.05) when compared to the ratio in healthy control (0.21±0.02), as clearly show in table (5). Since leptin and adiponectin are involved in the inflammatory process, these biomarkers might play some roles in prediction of chronic inflammations (Zaletelet al., 2010).

This resultisconsistent toresultreported by Jing Ling etal., (2014), who found that the higher serum leptin/adiponectin ratio in patientsthan that in healthy control, and they concluded that periodontitis could influence the level of adipokines in serum and change the leptin/adiponectin ratio.

Table 5: The differences in mean serum leptin\ adiponectin ratio among study groups.

Serum Adiponectin	Healthy control N=25	Periodontitis N=30	p-value
Range	**(0.01-0.73)**	**(0.01-3.98)**	**0<0.05**
Median	**0.15**	**0.31**	
Mean	**0.21**	**0.43**	
SD	**0.02**	**0.08**	

The results of correlation between leptin and adiponectin are clearly shown in figures (1). An anticipated, serum leptin level was showed significant negative correlation with serum adiponectin in patients (r=-0.325, p=0.011).

The imbalance between adiponectin (anti-inflammatory) and leptin (pro-inflammatory) in periodontitis determine the degree of inflammation which can lead to major clinical effects.

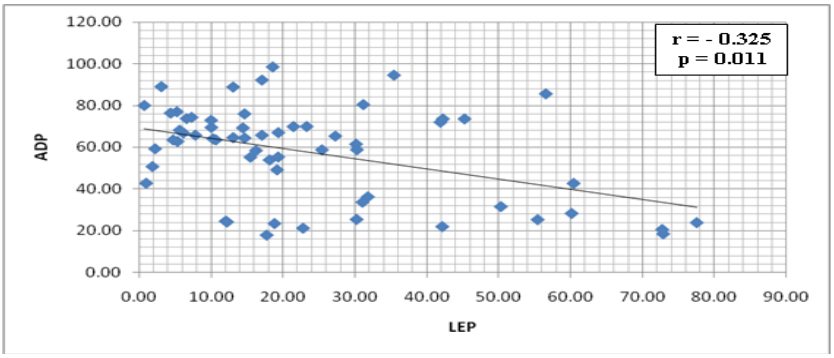

Figure-1: Correlation between leptin and adiponectin in periodontitis patients group

Finally, the current study did not observeany significantcorrelation between serum level of leptin, adiponectin, and ratio of leptin/adiponectin and clinical periodontal parameters (p>0.05), table (6, 7, 8).However; results of present study are at variance with other results reported by (Karam, 2013; Jing Ling et al., 2014), they stated 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 PPDand CAL, 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.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 conclusionthis study demonstrates that serum levels ofleptin and adiponectin play a crucial role in pathogenesis of periodontitis and the relative leptin/adiponectin ratio appears to be indicative of disease occurrence.

Table-6: 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-7: 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

Table-8: Correlation between Leptin/Adiponectin ratio and clinical periodontal parameters.

Leptin/Adiponectin	r-value	P-value
PI	0.137	0.469
GI	-0.083	0.663
PPD	0.057	0.764
CAL	-0.166	0.381
BOP	-0.127	0.503

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