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Assessment of Salivary Interleukin-1 Receptor Antagonist and Obesity Measures of Patients with Chronic Periodontitis in Comparison to Healthy Control

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ABSTRACT

Aim: *To measure BMI and waist circumference (WC) of patients with chronic periodontitis as well as healthy control, and to correlate these measurements with the clinical periodontal parameters, also to assess the level of salivary IL-1Ra of patients with chronic periodontitis in comparison to healthy control, to correlate the level of this marker with the clinical periodontal parameters and with anthropometric measurements (BMI and WC).* ***Materials and Methods:*** *Ninety subjects including both males and females with age between 35-55 years participated in this study. They were divided into two groups: Group 1 was chronic periodontitis (CP) group and it consist of 55 subjects and the Group 2 consist of 35 subjects as control group as they were with healthy periodontium and systemically healthy. Anthropometric measurements were measured for all participants, the whole unstimulated salivary sample was collected, and then periodontal evaluation that including the assessment of clinical periodontal parameters were done for all participants. ELISA was used to determine the level of IL-1Ra in saliva.* ***Results:*** *The results revealed a non-significant difference between the two groups regarding the BMI, while showed that there was a significant difference in WC between the two groups, that the mean value of WC was higher in chronic periodontitis group than the control group. Regarding the salivary level of IL-1Ra it was revealed that the mean value of salivary level of IL-1Ra was statistically higher in chronic periodontitis group than the control group and there was a highly significant difference between them. According to Pearson Correlation, this study showed that there is a strong positive correlation between clinical periodontal parameters (GI, BOP, PPD, and CAL) with BMI and WC. This study also revealed that there is a strong positive correlation between clinical periodontal parameters with salivary level of IL-1Ra. Also, it showed a strong positive correlation between salivary level of IL-1Ra with BMI and WC.* ***Conclusion****: This study offers evidence of relationship between clinical periodontal and obesity parameters therefore one condition may act as a risk factor for another as well as it showed relationship between salivary IL-1Ra and periodontal/obesity measures.*

Keywords: Periodontal disease, Obesity, IL-1Ra

Abbreviations: BOP: Bleeding on Probing; BMI: Body Mass Index; CAL: Clinical Attachment Level; CP: Chronic Periodontitis; ELISA: Enzyme-Linked Immunosorbent Assay; GI: Gingival Index; IL1-Ra: Interleukin-1 Receptor Antagonist; PPD: Periodontal Probing Depth; PLI: Dental Plaque Index; TNF-α: Tumor Necrosis Factor-α; WC: Waist Circumference

INTRODUCTION

Chronic periodontitis is an inflammatory disease. A main factor in its pathogenesis is the subgingival biofilm by its stimulation of immune responses that can leads to periodontal tissue destruction [1,2]. Moreover, susceptibility to periodontal disease can be modulated by genetic, environmental, and acquired risk factors that can result is an alteration in the host reactions [3,4].

Obesity is a condition that described to be associated with adipocytes expansion and amplified macrophage cells infiltration in the adipose tissues, outlining the inflammatory condition [5]. Considerable confirmation by the *in vitro* and *in vivo* studies has revealed the increase in susceptibility to periodontal tissue inflammation and destruction among overweight or obese subjects when they compared with healthy individuals [6,9].

Cytokines have taken a pronounced deal of research concern in the recent years. they are produce by a widespread range of cells as small regulatory proteins to control cell-cell interaction and other tasks particularly important for immune responses and inflammation [10], from these cytokines that establish to be related to both periodontitis and obesity is interleukin-1 receptor antagonist (IL-1Ra) which is one of the novel biomarker and is found as a natural anti-inflammatory protein and its represent a part of regulatory host response that inhibits IL-1 action that induced pro-inflammatory action [11].

MATERIALS AND METHODS

The participants in this study consist of 90 subjects, aged between 35-55 years old from both genders. The sample was collected from the patients who attended to the dental unit in Bader Health Center in Al-Kut city, Iraq. Collection of samples continued from the period between December 2016 and March 2017.

Ethics approval and consent to participate

The protocol was approved by the Institutional Ethics Committee. Informed consents have been assigned by all participants after they had been informed about the aims of the study.

Participants were grouped into two groups:

- **Chronic periodontist group (CP):** It consist of 55 patients with chronic periodontitis (Chronic periodontitis was defined by the presence of at least four sites with probing pocket depth ≥ 4 mm with clinical attachment loss equal or greater than 1-2 mm [12,13].
- **Control group:** It consists of 35 subjects with healthy systemic status and clinically healthy periodontium.

After initial periodontal examination, and before salivary sample collection and clinical examination, weight (in kilograms), height (in meters), and waist circumference (in centimetres) [14] were measured and registered. Calculation of the body mass index (BMI) was done by Quetelet Index, which is a value resulting from the individual weight and height. The definition of BMI is the body weight divided by the body height square, and it is expressed universally in kg/m^2 units, the resultant of mass (Kg)/height (meter). The measurement of the waist circumference (WC) of the individual was done by the use of measuring tape and the right place to make the WC measurement is midway between lowest rib and the highest of hipbone. The participant breathes out normally and we make certain that the tape is snug, without skin squeezing. Following that unstimulated whole saliva was collected according to Tenovuo and Lagerlof [15]. The patient drools the saliva passively in 10 ml centrifuge tube to collect 5 ml of saliva, and the sample was placed in the cooler box to be centrifuged later. After saliva has been collected a comprehensive periodontal examination was done to record periodontal health status which included:

- Amount of soft deposits was assessed according to Plaque Index by Silness and Loe [16].
- Gingival inflammation was assessed according to the criteria of Gingival Index system by Loe [17].
- BOP assessment according to Carranza [13].
- Assessment of PPD.
- Assessment of CAL.

Afterwards the sample was centrifuged at 3000 rpm for 20 minutes then preserved in plane tube and stored at −20°C in freezers to be analyzed later by ELISA kit for determination of salivary levels of IL1-Ra. The laboratory tests were done in laboratories of AL-KUT Hospital.

Statistical analysis

Statistical analysis was done using mean, SD, SE, percentages, Levene's test, t-test and Pearson correlation coefficient test (r).

RESULTS

A summary of the clinical periodontal parameters of the two groups were mentioned in Table 1.

Table 1 Summary for statistics of clinical periodontal parameters for CP and control groups

Parameters	Groups	N	Statistics			
			Mean		Std. Deviation	
PLI	CP	55	1.73		0.367	
	Control	35	0.53		0.238	
GI	CP	55	1.87		0.438	
	Control	35	0.33		0.238	
PPD	CP	55	4.68		1.05	
CAL	CP	55	4.18		1.454	
BOP	CP	55	Statistics			
			No.		%	
			Score 0	Score 1	Score 0	Score 1
			2338	2938	44.313	55.686

The mean value of BMI for the CP group (27.74 ± 4.985) was slightly higher than that of the control group (26.99 ± 4.093) and there was no significant difference between the two studied groups. The mean value of WC for the CP group (104.48 ± 12.916) was higher than that of the control group (98.42 ± 9.832) and there was a significant difference between the two studied groups. The mean value of IL-1Ra for CP group was greatly higher than that of the control group, the mean and Std. deviation were 625.51 ± 140.603 for the CP group, while they were 279.44 ± 60.678 for the control group and there was a highly significant difference between the two groups (Tables 2 and 3).

Table 2 Descriptive statistics of the mean values of BMI, WC, and IL1-ra parameters for the CP and control groups

Parameter	Groups	N	Mean	Std. Deviation	Std. Error
BMI	CP	55	27.74	4.985	0.672
	Control	35	26.99	4.093	0.691
WC	CP	55	104.48	12.916	1.741
	Control	35	98.42	9.832	1.662
IL1-ra	CP	55	625.51	140.603	18.958
	Control	35	279.44	60.678	10.256

Table 3 Statistical analysis of the mean values of BMI, WC, and IL1-ra parameters for the CP and control groups with comparison of significance

Independent Samples Test							
Parameter	Levene's Test for Equality of Variance			t-test for Equality of Means			
	F	P-value	Sig.	t	df	P-value	Sig.
BMI	0.82	0.368	NS	0.743	88	0.46	NS
WC	3.979	0.049	S	2.514	85.078	0.014	S
IL1-ra	28.193	0.00	HS	16.055	79.428	0.00	HS

According to Pearson correlation coefficient (r), there is a highly significant positive correlation between clinical periodontal parameters, GI (of chronic periodontitis and control groups), BOP, PPD, and CAL (of the chronic periodontitis group) with BMI, WC and salivary IL-1Ra, while there is non-significant correlation between the clinical periodontal parameter (PLI) of each group with the BMI, WC and salivary IL-1Ra (Tables 4, 5 and 6).

Table 4 Pearson correlation coefficient (r) between BMI and clinical periodontal parameter (PLI, GI, BOP, PPD, and CAL) of CP and Control groups

	Groups	Statistical analysis	PLI	GI	BOP	PPD	CAL
BMI	CP	r	0.059	0.645**	0.754**	0.453**	0.774**
		P-value	0.67	0.00	0.00	0.001	0.00
		Sig.	NS	HS	HS	HS	HS
	Control	r	0.024	0.497**	-	-	-
		P-value	0.891	0.002	-	-	-
		Sig.	NS	HS	-	-	-
** Correlation is significant at the 0.01 level (2-tailed)							

Table 5 Pearson correlation coefficient (r) between WC and clinical periodontal parameter (PLI, GI, BOP, PPD, and CAL) of CP and Control groups

	Groups	Statistical analysis	PLI	GI	BOP	PPD	CAL
WC	CP	r	0.045	0.776**	0.840**	0.551**	0.880**
		P-value	0.742	0.00	0.00	0.00	0.00
		Sig.	NS	HS	HS	HS	HS
	Control	r	0.033	0.581**	-	-	-
		P-value	0.853	0.00	-	-	-
		Sig.	NS	HS	-	-	-
** Correlation is significant at the 0.01 level (2-tailed)							

Also, there was a highly significant positive correlation between BMI and WC and salivary marker IL1-ra in chronic periodontitis and control groups (Table 7).

Table 6 Pearson correlation coefficient (r) between salivary IL-1Ra and clinical periodontal parameter (PLI, GI, BOP, PPD, and CAL) of CP and Control groups

	Groups	Statistical analysis	PLI	GI	BOP	PPD	CAL
IL-1Ra	CP	r	0.071	0.560**	0.625**	0.554**	0.744**
		P-value	0.605	0.00	0.00	0.00	0.00
		Sig.	NS	HS	HS	HS	HS
	Control	r	0.082	0.637**	-	-	-
		P-value	0.639	0.00	-	-	-
		Sig.	NS	HS	-	-	-
** Correlation is significant at the 0.01 level (2-tailed)							

Table 7 Person correlation coefficient (r) between obesity measures (BMI and WC) and salivary marker (IL1-ra) of the CP and Control groups

Parameters	Salivary markers	Groups	r	P-value	Sig.
BMI	IL1-ra	CP	0.604**	0.00	HS
		Control	0.518**	0.001	HS
WC		CP	0.711**	0.00	HS
		Control	0.739**	0.00	HS
** Correlation is significant at the 0.01 level (2-tailed)					

DISCUSSION

According to the results of this study the mean value of BMI is slightly higher in CP group but there is no significant difference between CP group and the control group, but there is great significant difference between CP and control group by waist circumference (WC) mean values. A recognized deficiency of BMI measurement is that it does not consider body composition nor the fat distribution. Regarding the fat tissue distribution, it has been detected that visceral fat accumulation has been shown to be more active metabolically and secrete much larger amounts of hormones and

cytokines compared with subcutaneous adipose tissue and has dangerous health effects [18]. Statistically significant differences have been observed in mean values of IL1-ra between the studied groups that a higher level of IL1-ra collected from periodontitis subjects, compared to healthy volunteers. According to one hypothesis, the production of IL-1Ra is a part of controlling host reaction; aiming to diminishing the activity of pro-inflammatory IL-1 [19]. This study showed that there is a highly significant positive correlation between clinical periodontal parameters (except for PLI) and obesity measures (BMI and WC). These associations were independent of variances in dental plaque levels and this finding continuous with previous study done by Suvan et al. [20]. The biological mechanisms underlying the association between obesity and periodontitis probably involve cytokines and hormones that derived from adipose tissue and collectively called adipokines that produces in a vast amount by the fat tissue, which include TNF-α [21] and leptin [22], which may modulate periodontal destruction [23,24]. Furthermore, it has been postulated that obesity reduces blood flow to the periodontal tissues, encouraging the advancement of periodontal disease.

CONCLUSION

In conclusion, the results showed a positive correlation between GI, BOP, CAL and PPD while there is non-significant correlation with PLI. These results suggested that there is a relation between salivary IL-1Ra level and the ongoing process of inflammation in the periodontal tissue. Periodontal bacteria may affect the network of cytokine in gingival fluid and periodontal tissues and by blocking the activity inhibitors. IL-1Ra was highly associated with obesity. Obesity is show a rise leptin level in blood, and is at present considered as adipocytokine of pro-inflammatory action [25]. In obesity, leptin effects may exert through the pathway of IL-1 and IL-1Ra may participate to resistance to central leptin. Discoveries showed that a major source of IL-1Ra is adipose tissue; as obesity-associated factors and inflammatory stimuli can be stimulating its secretion [26]. The secretion of IL-1Ra is typically by the fraction of adipocyte of adipose tissue and by the stromal fraction but at a minimum extent [27].

Recommendations

Larger sample sizes may be recommended to discover the diagnostic applicability of this biomarker.

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