Evaluation of Interleukine-1β (IL-1β) levels in Plasma of Patients with Periodontal Diseases and their correlation with Body Mass Index

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Abstract

Background and objectives: Obesity is emerging as a significant health problem worldwide and risk factor for various systemic diseases. Periodontal disease is multifactorial inflammatory disease. Recent evidence points to a link between body mass index and periodontitis, and role of Interleukin-1β (IL-1 β) has been suggested.

Materials and methods: One hundred and sixty subjects were divided into two groups: 80 healthy subjects as a control group and 80 patients with periodontitis. Their age ranged from 25 to 45 years. Then subjects of both groups were subdivided in to four subgroups based on the WHO classification of Body Mass Index(BMI): group A; Under-weight (BMI< 18.5kg/m^2), group B; Normal-weight (BMI 18.5-24.95 kg/m^2), group C; Over-weight (BMI 25-29.95kg/m^2) and group D; Obese (BMI >30 5kg/m^2). Full-mouth periodontal assessment was performed and Clinical periodontal parameters included clinical attachment level (CAL) and probing pocket depth (PPD). The quantitative assay of IL-1β was performed in serum, using an ELISA method. The BMI, IL-1β levels in plasma and periodontal Disease Index (PDI) scores were assessed, compared and correlated.

Results: In patients with periodontitis, significantly higher clinical periodontal parameters (CAL and PPD) and IL-1β levels were found in obese subgroup as compared to other subgroups. Also, a significant and positive correlation was seen between BMI and IL-1β, CAL and PPD, while correlation coefficient between mean scores of PPD, CAL and mean concentration of IL-1β in sera were statistically highly significant and negative respectively. In control subgroups, a highly significant increased level of IL-1β was observed in sera of obese subgroup when compared to other subgroups.

Conclusion: Increase in the level of IL-1 β in sera and an increase in the severity of periodontitis seen in subjects with higher body mass index. This may indicate that obesity may be detrimental to the periodontal health of individuals.
Key words: Periodontitis; BMI, Interleukine-1β (IL-1β).

INTRODUCTION

Periodontitis, is a chronic inflammatory disease of the periodontium occurring in response to bacterial plaque on the adjacent teeth; characterized by destruction of the alveolar bone and periodontal ligament, apical migration of the epithelial attachment resulting in the formation of periodontal pockets, and ultimately loosening and exfoliation of the teeth [(1)].
Obesity is a complex multifactorial chronic disease that develops from an interaction of genotype and the environment among obese subgroups. Obesity has a significant association with periodontitis in terms of body mass index (BMI). The BMI has always been considered a simple method for analysis of the nutritional status. These findings suggest that periodontitis may be aggravated by certain conditions associated with obesity for example, "the metabolic syndrome", a clustering of dyslipidaemia and insulin resistance [(2)].

It is now clear that adipose tissue is complex and metabolically active. It secrets numerous immunomodulatory factors and plays a major role in regulating metabolic and vascular biology. Adipose cells secrete more than 50 bioactive molecules, known collectively as adipokines which include Interleukine-1Beta (IL-1β), which may inhance periodontal degradation [(3)].

IL-1β is a pro-inflammatory cytokine that plays a pivotal role in several chronic diseases produced by monocyte, macrophage, and epithelial cells[(4)].This cytokine is a primary activator of early chemotactic cytokines, as well as of the expression of adhesion molecules that facilitate migration of leucocytes in to tissues. IL-1β is also known to be one of the most active stimulators of osteoclastic bone reabsorption [(5)].

IL- 1β stimulates a variety of cell types to produce connective tissue catabolic and bone-resorptive mediators, including IL-6, TNF-α, prostaglandin E2, and matrix metalloproteinase [(6)] .These factors lead to the degradation of connective tissue such as collagen, along with the recruitment and activation of osteoclasts. Much attention has been given to the influence of IL-1β on bone turnover, particularly in pathologic disease processes such as periodontitis [(7)]. IL-1β has been shown to have a dual function in collagen digestion. It inhibits the intracellular phagocytic pathway, but at the same time strongly promotes extracellular

Iraqi Dental Journal Volume:34 Issue:2; 2012

digestion by inducing the release of collagenolytic enzymes such as collagenase [8].

Data indicate that increased body mass index, serum adipokine levels and percentage of subcutaneous body fat are associated with increased risk for periodontitis. For instance, more bleeding on probing, deeper periodontal pockets and more bone loss were noticed in individuals with higher indicators of obesity [9].

Additionally, increased amounts of adipokines (e.g.1L-1β, TNF-α, Leptin) from visceral fat may induce agglutination of blood in the microvasculature, decreasing blood flow to the gingiva in obese people and facilitating the progression of periodontitis. Despite the accumulating evidence for significant associations, it is still unclear whether obesity truly precedes periodontitis. However, maintaining a normal body weight, eating a well-balanced diet and engaging in physical activity have been shown to reduce the severity of periodontitis [10].

Periodontal disease is no longer identified as only an oral health problem but also a public health issue as it is associated with systemic health. Many mediators have been recognized for this relationship like chronic inflammation, infection and genetic predisposition. Apart from these mediators, nutrition has been postulated as an alternative mediator[11]. High body mass index, the most common nutritional disorder, is a significant risk factor for numerous adult diseases, and may be a factor in the incidence of periodontitis [12].

The link between BMI and periodontal disease may not be completely understood, but it is clear that once established, this relationship will prove to be of extreme public health relevance. It may go a long way in planning and modifying preventive and treatment modalities for periodontal disease. Hence this study was planned to evaluate the relationship between BMI, 1L-1β, and periodontal disease.

MATERIALS AND METHODS

A cross-sectional study on association between periodontitis with BMI in Erbil city province was carried out. Study subjects were recruited from department of periodontology, College of dentistry, Hawler Medical University in Erbil city. The data was collected during the period of 10th January up to 17th May 2011.

A total One hundred and sixty subjects have been included in this study, 80 healthy subjects that represented a control group and 80 patients with periodontitis that represented the study group. Their age ranged from 25 to 45 years. They were selectively included during their visit to the department of periodontics. Then subjects of both groups were subdivided in to four subgroups based on the WHO classification of Body Mass Index: group A; Under-weight, group B; Normal-weight; group C; Over-weight and group D; Obese. All patients were systemically healthy. This study involved height and weight measurements for determination of BMI, done by ourself and another assistant. A structured questionnaire was completed by each subject. Dental examinations were carried out by experienced periodontist. Blood samples were collected after an overnight fasting. Those selected were categorized into 4 subgroups, as summarized in (Table 1). Ethical approval was obtained from the College of Dentistry/Hawler medical university in Erbil city. Informed consent obtained from participants who were classified as under-weight, normal weight, over-weight, and obese according WHO classification. Inclusion and Exclusion criteria are presented in (Table 2).

Table (1): Flow table illustrated the number of groups and subgroups of control and patient with periodontal condition associated with BMI.

Groups / Sub-groups	Periodontitis N=80	Control N=80	BMI(kg/m²)
A	20 Under-weight	20 Under-weight	< 18.5
B	20 Normal weight	20 Normal weight	18.5 - 24.9
C	20 Over-weigh	20 Over-weight	25 - 29.9
D	20 Obese	20 Obese	≥ 30

Table (2): Flow table illustrated Inclusion criteria and Exclusion criteria

Inclusion criteria	Exclusion criteria
Age (25-45).	Current alcohol and smokers
Systemically healthy.	Prior antibiotic used one week before the study
Clinical attachment loss ≥ 4mm	Prior use of systemic corticosteroids within the last month
Number of teeth ≥ 10 teeth	General dental scaling in the last month
	Systemic diseases. e.g. DM, hypertension, CVD
	Current medications influencing the periodontal tissues within the last month.
	Current pregnancy

Probing pocket depth (PPD): The distance from the gingival margin to most apical extent of Williams probe inserted in to gingival crevice as close as possible to the long axis of tooth at four surfaces of each tooth was recorded in millimeter (mm) [13]. The sites for measurement were mesio-buccal, mid buccal, disto-buccal, mid-lingual lines. No pressure was used the probe was allowed to fall by its own weight.

Clinical attachment loss (CAL): This was assessed by measuring the distance from the cement-enamel junction (CEJ) to the base of the pocket [13], the level of CEJ could be determined detecting it with a probe [14], when CEJ was obliterated by the gingival margin, the CAL was measured indirectly by subtracting the distance in millimeters from the gingival margin to the CEJ from PPD at each site. In cases when there was a gingival recession, loss of attachment was measured by adding the distance from the gingival margin to the CEJ to PPD at each site [15]. The criteria for periodontitis in the present study was defined by patient who had two or more interproximal sites with CAL of 4mm or more (not in the same tooth) non djacent teeth and (PPD ≥ 4mm) [16].

Body mass index (BMI): was used to indicate overall adiposity (kg/m^2). It was calculated using each participant's weight in (Kgs) divided by the (m^2).

$$BMI = \frac{\text{Weight in (Kgs)}}{\text{Height in (m}^2\text{)}}$$

The recommended WHO Standard BMI classification was applied in this study.

Blood Samples and Processing

Blood samples were collected after an overnight fasting. Venous blood samples were obtained from enrolled subgroups by vein puncture five milliliter was withdrawn from each patient and control subgroups. Five ml were collected into sterile plain tubes; the blood was left for a while at room temperature to clot. Then it was centrifuged at 2500 rpm for 10 min, the serum was separated and transferred into sterile screw capped labeled tubes and stored at – 20C°. The stored plasma was used for estimation of IL-1β levels at a later date using an enzyme immunoassay for the in vitro determination of IL-1β in plasma. The assay was carried out as per manufacturer's directions for use by the commercial **KOMA BIOTECH INC** IL-1β ELISA kit (**Seol , Kores**).

Statistical analysis

The collected data were analyzed by using Computer program software SPSS (Statistical Package for Social Sciences); version **15** (www.spss.com).

1- Descriptive statistics which include: Mean; Standard deviation; Tables, Multiple Dot Diagram and Column chart.

2- Inferential statistics which included:

a- Post-Hoc Comparisons to see exactly which groups are significantly different.

b- T-test used for statistically significant difference between group mean was tested.

c- The Pearson correlation coefficient was used to analyze linear relationship of each two variables. Results were considered significant, if P value ≤ 0.05.

Iraqi Dental Journal Volume:34 Issue:2; 2012

RESULTS

For the clinical periodontal parameters, from (Table 3) showed a descriptive statistics of the mean scores and standard deviation of periodontal parameters (CAL and PPD) for four periodontitis subgroups (under weight, normal, over and obese weight), it has been shown that the mean of CAL for obese subgroup was highest one which was (5.70 ± 0.62), than Under, Normal, Over weight subgroups which were (4.49 ± 0.16, 4.78 ± 0.30, 5.17 ± 0.52) respectively, and also PPD for obese subgroup was the highest one which was (4.35 ± 0.38), when compared with Under, Normal, Over weight which were (4.0 ± 0.16, 4.10 ± 0.21, 4.20 ± 0.34) respectively. Indicated that the mean scores of CAL and PPD in obese subgroup was greater and decreased with decreasing in BMI. Figure (1 and 2) showed mean and standard deviation of clinical periodontal parameters (CAL and PPD) in each periodontitis subgroups with total mean and standard deviation for all periodontitis subgroups together in relation to BMI.

Regarding the periodontitis subgroups, the mean concentration of IL-1β in obese subgroup was (7.83pg/mL) while declined in over-weight, normal weight and under-weight were (5.46, 4.16, 3.078 pg/mL) respectively. Regarding control subgroups, the same table showed a marked increase in mean concentration of IL-1β in obese subgroup (3.45 pg/mL) when compared with under weight, normal and over weigh control subgroups which were (2.57, 3.32 and , 3.31, pg/mL) respectively

Results obtained from (Table 4), showed that the mean concentration of IL-1β, was higher in high BMI category than in low BMI category in both periodontitis and control groups, and high in periodontitis group than control group, the same findings were more clear in (**Figure 3**).

By using Post Hoc Test as demonstrated in (Table 5), indicated that there were a highly significant difference in mean scores of CAL between obese weight and overweight ($p<0.001$), however, there were non significance difference in mean scores of PPD between this two subgroups ($p>0.05$). As shown from the same table there were highly significant differences in mean scores of CAL and PPD between obese and normal weight ($p<0.001$, $p<0.01$) respectively. While, there were highly significant difference in mean scores of CAL and PPD between obese weight and under weight ($P<0.001$, $P<0.01$) respectively. Whereas, highly significant differences in serum IL-1β level between obese weight and normal weight ($P<0.001$). Similarly, highly significant difference in serum IL-1β, was observed between obese weight and under weight ($P<0.001$).

Results illustrated in (Table 6), by using Post Hoc Test showed that statistically highly significant differences in serum IL-1β levels ($P<0.001$) between obese weight and under weight. The same data showed a highly significant differences in serum IL-1β levels between obese weight and normal weight, obese weight and over weight ($P<0.001$ and $P<0.001$) respectively.

By Pearson correlation coefficient analysis, for obese weight periodontitis subgroup, analysis the correlation between the mean scores of PPD and mean scores of CAL was ($r=0.594^{**}$, $p<0.05$) were highly significant and positive. Correlation coefficient between mean scores of PPD, CAL and mean concentration of IL-1β in sera ($r=-0.694^{**}$, -0.644^{**}, $P< 0.01$) were statistically highly significant and nnnnegative, respectively (Table 7).

Table 3: The descriptive statistics for the clinical periodontal parameter (CAL and PPD) in periodontitis subgroups in relation to BMI.

Variables	types of weight	N	Mean	Std. D.	Std. E.
CAL(mm)	Under-weight	20	4.49	0.16	0.362
	Normal weight	20	4.78	0.30	0.067
	Over-weight	20	5.17	0.52	0.115
	Obese	20	5.70	0.62	0.139
	Total	80	5.03	0.63	0.070
PPD(mm)	Under-weight	20	4.00	0.16	0.036
	Normal weight	20	4.10	0.21	0.045
	Over-weight	20	4.20	0.34	0.076
	Obese	20	4.35	0.38	0.084
	Total	80	4.16	0.309	0.035

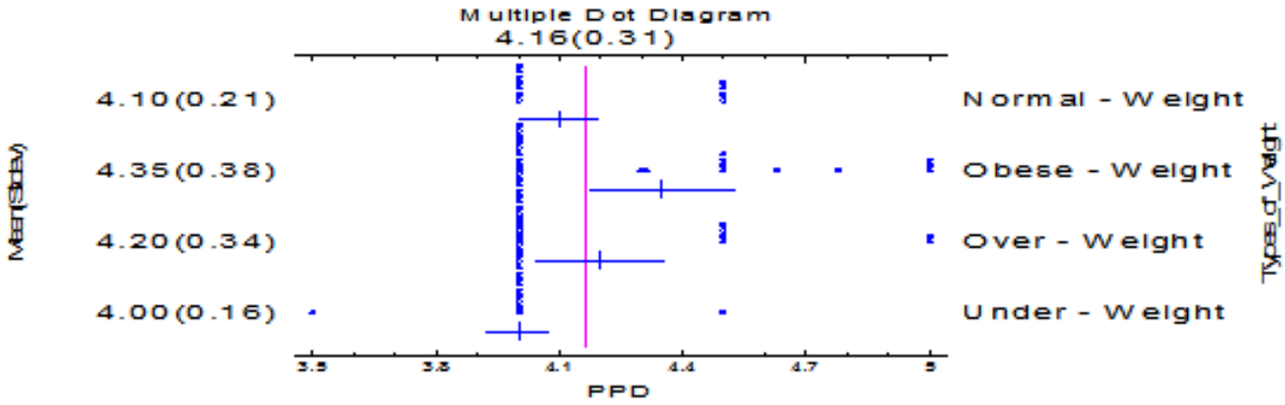

Figure 1: Multiple Dot Diagram demonstrated mean scores and standard deviation of periodontal parameters (PPD) in each sub-group with total mean and standard deviation in all periodontitis subgroups together in relation to BMI.

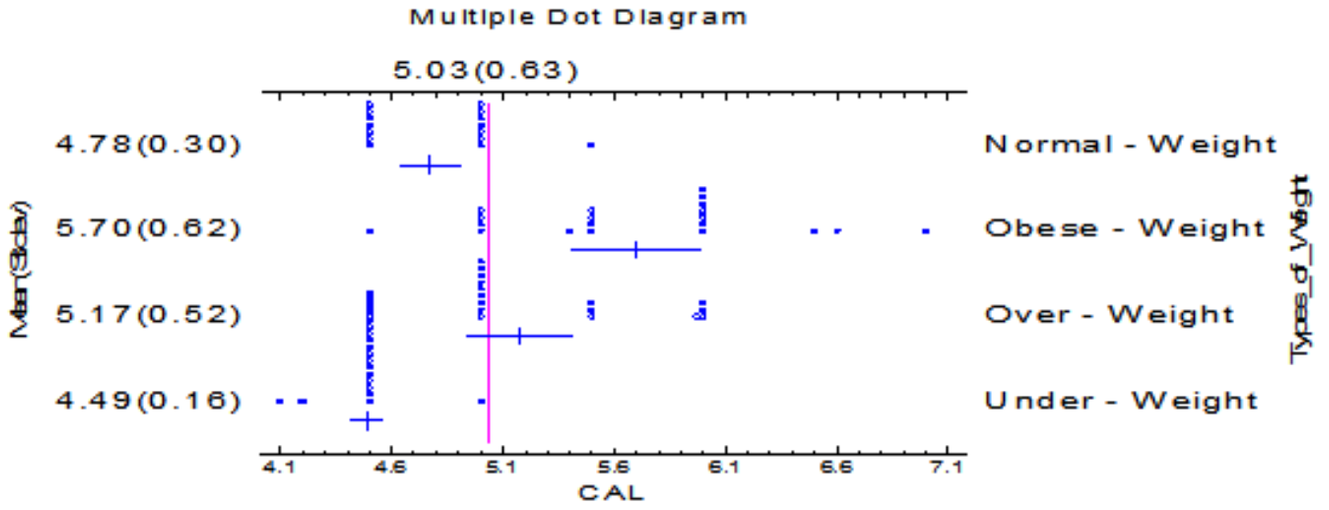

Figure 2: Multiple Dot Diagram demonstrated mean scores and standard .deviation of periodontal parameters (CAL) in each subgroup with total mean and standard deviation in all periodontitis subgroups together in relation to BMI.

Table (4): The descriptive statistics for the mean concentration of serum IL-1β (pg/ml) in each of periodontitis and control groups according to BMI.

Serum cytokine	Groups	Under-weight Mean ± S.D.	Normal-Weight Mean ± S.D.	Over-Weight Mean ± S.D.	Obese Mean ± S.D.	Total N=160 Mean ± S.D.
IL-1β (pg/ml)	Periodontitis Subgroups N=20	3.08 ± 0.82	4.16± 1.24	5.46± 0.96	7.83± 1.67	5.13± 2.15
	Control Sub-groups N=20	2.57± 0.36	3.32±0.95	3.31±0.89	3.45 ± 1.07	3.14± 0.91

Iraqi Dental Journal Volume:34 Issue:2; 2012

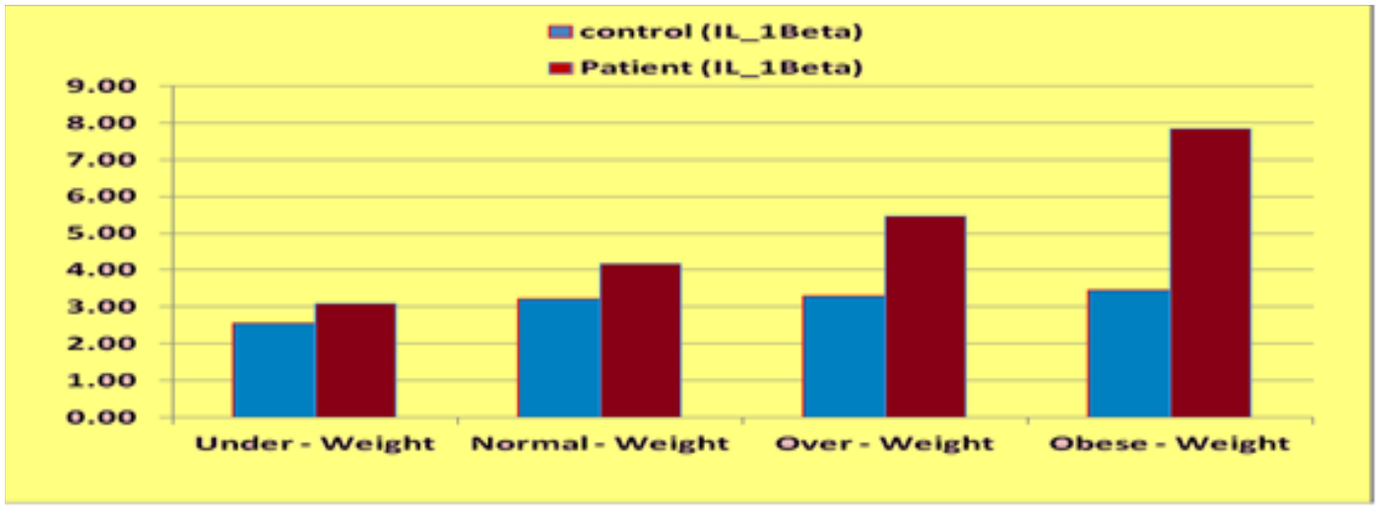

Figure 3 : Column chart for detection of mean concentration of IL-1β (pg/mL) in sera for both periodontitis and control subgroups in relation to BMI.

Table 5: Comparison of Obese-weight periodontitis subgroup with other periodontitis subgroups (Under-weight, Normal-weight, Over-weight) by Post Hoc Test.

Dependent Variable	(I) type of weight (kg/m^2)	(I) type of weight (kg/m^2)	Mean difference (I-J)	Std. Error	Sig.
PPD (mm)	Obese	Under-weight	0.351	0.091	0.004**
		Normal-weight	0.251	0.091	0.007**
		Over-weight	0.151	0.091	0.099^N
CAL(mm)	Obese	Under-weight	1.210	0.139	0.000**
		Normal weight	0.925	0.139	0.000**
		Over-weight	0.527	0.139	0.000**
IL-1β (pg/ml)	Obese	Under-weight	4.756	0.385	0.000**
		Normal weight	3.672	0.385	0.000**
		Over-weight	2.372	0.385	0.000**

Table 6: Comparison of Obese-weight control subgroup with other control subgroups (Under-weight, Over-weight, Obese weight) by Post Hoc Test.

Dependent Variable	(I) type of weight (kg/m^2)	(J) type of weight (kg/m^2)	Mean difference (I-J)	Std. Error	Sig.
IL-1β (pg/ml)	Obese	Under-weight	0.873	0.273	0.002**
		Normal-weight	0.215	0.273	0.434N
		Over-weight	0.133	0.273	0.629N

Table 7: Correlation between periodontal scores (CAL and PPD) and serum IL-1β level in obese weight periodontitis subgroup.

Variables	PPD (mm)	CAL (mm)	IL-1β (pg/ml)
PPD Pearson correlation	1	0.595**	-0.694**
Sig. (2-tail)		0.006	0.001
N	20	20	20
CAL person correlation	0.595**	1	-0.644**
Sig. (2-tail)	0.006		0.002
N	20	20	20
IL-1β Pearson correlation	-0.694**	-0.644**	1
Sig. (2-tail)	0.001	0.002	
N	20	20	20

DISCUSSION

It has been suggested that obesity contributes to an overall systemic inflammatory state through its effect on metabolic and immune parameters, thereby increasing susceptibility to periodontal disease [17]. In recent years, the evidence linking obesity to increased incidence and severity of periodontal disease has grown [18].

Increasingly, evidence of a relationship of newly identified risk factors for systematic diseases to periodontal disease is starting to emerge. In this light, recent studies indicate that obesity is emerging as a risk indicator for periodontal disease [19]. In this study, the correlation between serum IL-1β level and periodontal disease in relation to BMI has been evaluated. Studies have shown that obese subjects have abundant cytokines in the serum due to cytokine release from adipose tissue [20]. It may be speculated that the raised serum cytokines are transported at higher levels in to the gingival tissue [21] .

The periodontal parameters in present study were clinical attachment loss and probing pocket depth. The present findings showed a statistically significant correlation between BMI and periodontal measurements of CAL, and PPD. The severity of both clinical attachment loss (CAL) and probing pocket depth (PPD) was significantly associated to BMI. This study confirms that the severity of CAL and PPD, specially the severity of CAL was higher in both obese and over-weight subgroups than other two subgroups which were normal and under-weight.

In this study, increased in the severity of CAL and PPD with increasing in BMI corresponds with the work by team workers; they founded that increased BMI were found to be significantly associated with the presence of CAL and PPD, [18].

Our findings are similar to those of cross-sectional study by [9], found that there is a significant correlations between BMI and mean of CAL and PPD. Ylöstalo and coworkers (2008) [22] reported a strong association between BMI and the presence of pockets. Moreover,[23] concluded overweight and obese individuals that might put them at risk for initiation and progression of periodontitis and risk was significantly higher in obese individuals.

The relationship between BMI and periodontal variables was showed by [24] were in contrast to the results of present study was significantly no associated present between CAL, PPD and BMI,

Increase in BMI associated with periodontitis, high BMI has been postulated to reduce blood flow to the periodontal tissues, promoting the development of periodontal disease[25]. Furthermore, high BMI may enhance immunological or inflammatory disorders, which might be the reason for obese subjects, tend to exhibit escalating poor periodontal status relative to non-obese individuals [19]. Furthermore, it has been shown that adipose tissue secretes several proinflammatory cytokines, also implicated in periodontitis[24]. As host response to local bacterial challenge is a key factor in determining periodontitis susceptibility, an increased inflammatory state as that found in obese individuals could predispose them to increased periodontal tissue destruction [27].

The present study demonstrated that periodontitis was significantly associated with serum

Iraqi Dental Journal Volume:34 Issue:2; 2012

level of IL-1β when compared with control subject, and also a highly statistically significant elevation of serum concentration of IL-1β were observed in those with the highest quartile of BMI compared to those in the lowest quartile because obesity is likely to result in greater IL-1β production. A study was done by Boch and co-workers (2001)[28] corroborated above mentioned finding of IL-1β levels as a biomarker of periodontal disease. Elevated levels IL-1β was found to significantly increase the risk of periodontal disease. The levels of IL-1β could serve as biomarkers of periodontitis. IL-1β levels have been reported to be elevated in periodontal tissues in high BMI when compared to low BMI. A study done by Gamonal and colleagues (2003)[29] similar to our results showed that the evaluation of the IL-1β was performed comparing periodontal patients and individuals without disease. There was a significant difference in IL-1β when comparing the high BMI subgroup with the low subgroup. Ziccardi and co-workers (2002)[30] stated that obese and over-weight individuals have raised levels of circulating IL-β compared with those of normal weight, with some reduction in cytokine levels on weight reduction, this is agree our results and with Saxlin and co-workers (2009b)[31] suggested that there was a significant association between periodontitis and an association between serum IL-l-β, body weight and periodontitis.

In contrast to our findings Hodge and co-workers (2001)[32] and Tai and colleageus (2002) [33],who observed no significant differences in the serum IL-1β levels between periodontitis, control subgroup and BMI in European and in Japanese individuals, respectively. This was due to their study design, which was recruited higher range of age and their definition to periodontitis was different from the definition used in this study

In obese periodontitis subgroup, Pearson correlation coefficients of CAL and PPD with obesity were determined in present study. The results demonstrated a highly significant positive correlation ($P< 0.01$). The results of our study were similar to those reported by, (Saito and Shimazaki, 2007) [34], they found a highly significant positive correlation between obesity and periodontitis. Whereas highly negative correlation were found between CAL, PPD and IL-1β ($r=-0.694^{**}$, -0.644^{**}, $P< 0.01$), disagree with results of, (Ikezawa-Suzuki et al., 2008)[35], this may due to the design of their study and definition of periodontitis

Our results confirm those reported by[36] whom concluded that severity of periodontal disease could be evaluated through IL-1β activity. Identified IL-1β as playing a pivotal role in the pathogenic mechanism of periodontal tissue destruction. According to the authors, clinical parameters such as probing depth (PD). Moreover, the degree of inflammation within periodontal disease tissue could be measured IL-β activity in diseased tissues based on the classification of clinical parameters.

CONCLUSION

Clinical attachment and probing pocket depth appear to be highly significant in obese subgroup when compared with other subgroups. Serum IL-1β level appear to be high in case of periodontitis than control subgroups. Our study strengthens the idea of higher of proinflammatory cytokine IL-1β concentrations in sera in high BMI subgroup relative to low BMI subgroups. This indicated that obesity may be detrimental to the periodontal health of individuals.

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