

## Salivary Interleukine 6 and its role on developing periodontitis

Thana Mohammed Juda<sup>1</sup>, Mahdi.y.Kzar<sup>2</sup>, SennaBeder<sup>3</sup>, Khalil Ibrahim Zaidan<sup>4</sup>

<sup>1</sup>Babylon university /college of medicine, <sup>2</sup> University of Babylon /Dentistry college,  
<sup>3</sup>University of Babylon /college of medicine, <sup>4</sup> Babylon university/Dentistry college.

E mail: [thanaswedi@yahoo.com](mailto:thanaswedi@yahoo.com)

### Abstract

**Back ground** Interleukin-6 (IL-6) is biologically active small protein molecules known as cytokines .These cytokines are produced by leukocytes, adipocytes, and endothelial cells, and it is involved mainly in inflammatory processes. IL-6 has a role in stimulating the immune response as trigger to infection or trauma through the production of acute-phase proteins that accompany the inflammatory process. IL-6 synthesized according to code from messenger RNA, so their production in tissue in response of inflammation are increased by the action of increasing expression of its own specific messenger RNA and the expression levels of the mRNAs were either up- or down-regulated by adjacent focal infiltrating lymphoid cells according to the state of periodontal in health and disease so the local concentration of cytokines reflect the state of inflammatory process under control at nuclear level.

The aim of study is to evaluate the inflammatory cytokine that associated the process of periodontitis

**Methods:** Salivary specimens were obtained from patients having chronic periodontitis and healthy subject act as control group. The assessment of IL6 concentrations were established by technique enzyme linked immunoassay.

**Results:** level of IL-6 in saliva sample after evaluation the result showed statistically significant difference between patients and control .

**Conclusions:** The result obtained from this study revealed that estimated salivary IL 6 can be used in management protocol of process of periodontitis

**Key words:** saliva , interleukin 6 (IL6), periodontitis .

## **Introduction**

Periodontitis is an inflammatory disease effect mainly the cementum, bone, and periodontal ligament which act as supporting structures of the dentition .The gingival sulcus and coronal connective tissue is considered the primary start point of periodontitis . With time when the disease process continue in progression can result in periodontal attachment loss and bone destruction.(1,2).

The etiology of Periodontitis as chronic inflammatory disease is considered multifactorial in origin and it initiated by specific bacteria when invade tissue it will lead to activate host mechanisms process which as result of this interaction network will caused in destruction the bone and connective tissues that support the teeth(3-5) .

In recent years, studies which done on periodontitis have revealed that is associated with elevated levels of inflammatory cytokines which have a role on developing substantial and various biological activities, and they take part in triggering the inflammatory cascades phenomena and systems (6,7).

The cytokines are multifunctional proteins and considered as category of glycoproteins (which are protein interact with carbohydrate ) that involved in process of communication between cells and also regulation the function intercellular by acting as organized factors important for completion function of cell and communication of cell with other cell at both local and systemic level which considered as local hormones . these cytokines are manufactured by immune cells mainly T lymphocytes and monocytes in local inflammatory tissue infiltrates. Periodontal tissue components such as fibroblasts and epithelial and endothelial cells all participate in cytokines secretion that accompany the inflammatory process (8).

Periodontal health process depends on the local balance among reactive and suppressor immune cells, their cytokines and mediators ,the all process of inflammation is depend on interaction between two types of cytokines the activator and suppressor . Cytokines types of IL-6, IL-8 and IL-12 have pro inflammatory functions, and induce bone reabsorption

(9). on other hand the IL-10 has anti inflammatory effects opposite the process of pro inflammatory cytokine (10).

The inflammation and destruction processes which involved periodontal disease result from the host immune response to bacterial invasion. Bacteria and lipopolysaccharide (LPS) bacterial element may trigger the production of inflammatory mediators, such as cytokines, by activated macrophages and fibroblasts present in periodontitis lesions. Several bacteria including *Actinobacillus actinomycetemcomitans* (Aa) and *Camphylobacter rectus* (Cr) have been shown to amplify human host inflammatory reactions mediated by pro-inflammatory cytokines, including IL-6 and IL-1 (11,12).

IL-1, IL-6, and TNF- $\alpha$  are considered a master key mediators in inflammation process. These cytokines cause systemic effects such as increased body temperature, neutrophil mobilization, and increased lymphocyte activation.(13,14) They are of particular importance due to their role in the acute-phase response...The pathogenesis of periodontitis involves more than virulent microorganisms so there are other important factors as the systemic immune response, genetic factors, and environmental factors also play a role in increasing the risk of developing periodontitis. In recent years, studies have demonstrated that periodontitis is associated with increase levels of a different inflammatory elements. Furthermore, genetic variants of some cytokines are associated with increase the risk the susceptibility to develop periodontitis (15,16).

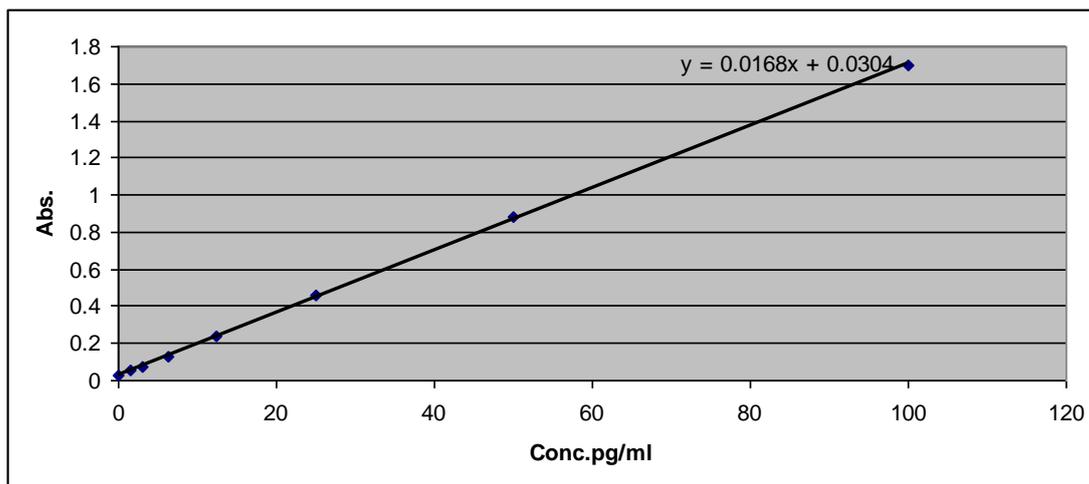
### **Material and method:**

#### Selection groups

Group 1: patients with chronic periodontitis attending special dental clinic and diagnoses by specialist dentist according to criteria of chronic periodontitis diagnosis by special dentist.

Group 2: Healthy persons act as control groups

Saliva samples were collected, Participants were asked to abstain from eating, chewing and drinking at least one hour before collection. Saliva was collected into plain tubes by drooling method. Samples were frozen and kept at -70 °C until the time of analysis. After defrosting, saliva samples were centrifuged then analyzed within 1-2 hours. Salivary IL6 level were analyzed by technique enzyme linked immunoassay (ELISA, USA). and the standard curve for estimation of IL-6 in Pg/ml. were represented in figure 1.

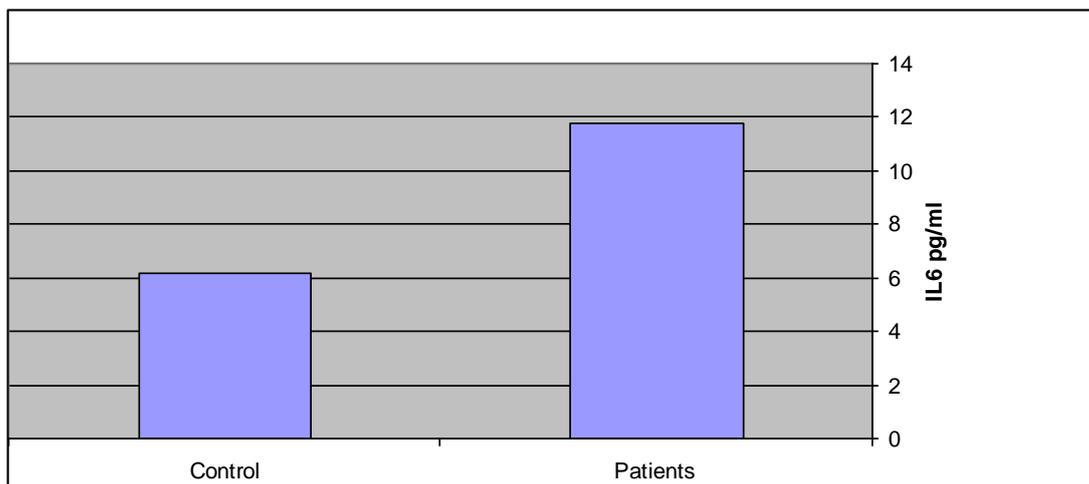


**Figure (1): standard curve for IL6.**

Statistical analysis were performed using SPSS17:0(SPSS Inc,Chicago ,11,USA ) using student t- test for comparisons between the groups. P-Values lower than 0.05 ( $p < 0.05$ ) were considered as statistically significant.

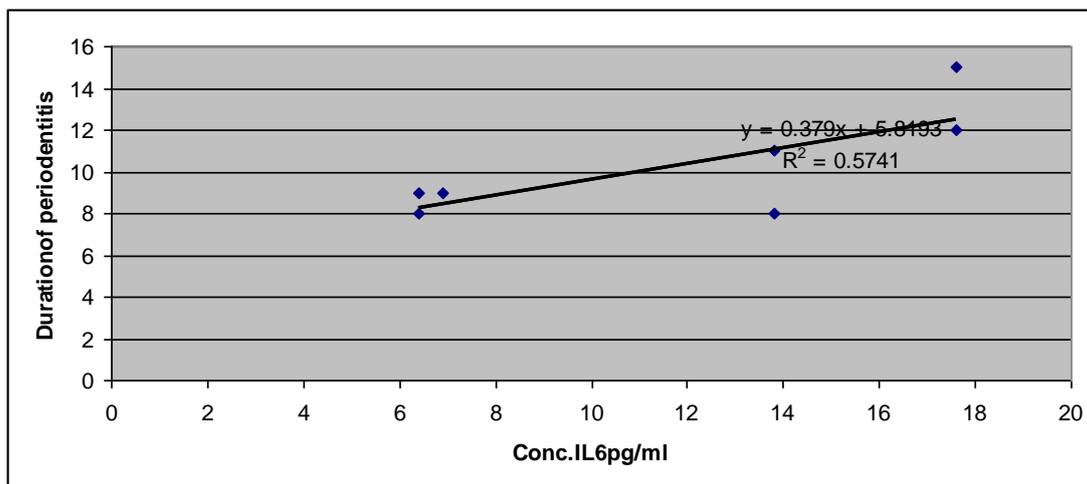
## Result

The mean of IL6 level in patients and control are 11.2 pg/ml and 6.2 pg/ml respectively and the results are representing in figure no.2



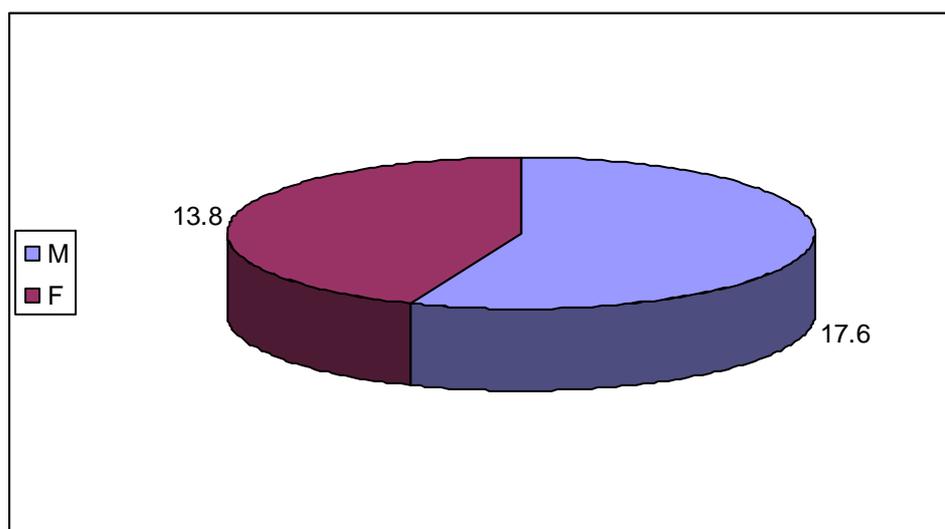
**Figure (2): IL6 mean in patients and control.**

The relation between IL6 and duration in periodontitis are representing in correlation as shown in figure no.3



**Figure (3): correlation between IL6 and duration of periodontitis**

The mean of IL6 among males patients with periodontitis was 17.8pg/ml and among female was 13.8 and the results representing in figure no.3



**Figure (4): Mean concentration of IL6 among males and females.**

## Discussion

Inflammatory responses accompany the disease considered as protecting process against periodontopathic bacterial invasion [17,18] .

Interleukin-6 is glycoprotein has multifunction properties because it is behavior in both process of signaling and the signal transducer [19, 20].

Recent studies have shown that there are increasing in the level of IL-6 that accompany the developing the process of periodontitis in comparison with its level in healthy groups [21, 22]

Salivary IL-1 and IL-6 significantly increased with the development of periodontitis. These two cytokines which considered as pro inflammatory factors are sensitive to pathogen invasion and can reflect the severity of periodontitis. In addition, pro inflammatory cytokines significantly increased with the severity of periodontitis, and stimulated IL-6 was found to be an effective marker for assessment the effectiveness of periodontitis management regimes. The estimated IL-6 can give idea about the improvement of periodontitis with starting of management the disease so can assess the all protocol used in treatment of periodontitis .

Currently ,there is requirements for definitive test which can be valid as diagnostic measure and also used for follow up the patients with periodontitis to know the stage of developing and whether the periodontitis progress or regress with time and with treatment ,this definitive test can be used as additive test beside the routine clinical diagnosis of periodontitis which mainly depending on visual and radiographic evaluation of pocket depth, tissue attachment, and “bleeding on probing” (BOP) in which is established in dental practice and this follow up taking time to show the changes of periodontitis in response to management regimes [23]. The dentist need a reliable test beside his conventional diagnostic procedure which used in evaluation of periodontitis as oral diagnosis and x ray and probing assessment and this test depend on biochemical changes in content of saliva which accompany the process of developing and progression of periodontitis and this analysis of saliva are used to reflect the whole process of inflammation and secretion of cytokines from inflammatory cell that accompany the process of inflammation and this biomarker can be used as diagnostic criteria in assessment of developing the process of periodontitis(24) .

The information which obtained from the process of evaluation the condition of patient and analysis of this information are considered central aspect of effective clinical assessment of developing the process of periodontitis [17]. Lack of evidence-based information of patients’ disease can cause clinical mismanagement, for example, failure to identify disease activity and inappropriate antimicrobial therapy [25]. The requirement for reliable biomarkers to distinguish progressive periodontitis is considered fundamental to identify periodontitis at an earlier or even preclinical stage, to initiate preventative aspect, and also to conduct epidemiological studies (26).

This study revealed there is significant difference in mean of IL-6 among patients with periodontitis in comparison with control at P Value  $<0.05$ , which indicate that IL6 considered as a biomarker in developing periodontitis and the result indicating that there is positive correlation between IL6 and duration of periodontitis which prove the severity and chronicity of periodontitis .

The study shown there is no effect of gender on level of IL6 in periodontic patients. The correlation between IL6 and progression of periodontitis proved by other studies (27,28).

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#### **Abbreviations list:**

Aa: *Actinobacillus actinomycetemcomitans*; Cr: *Camphylobacter rectus*;

ELISA:enzyme linked immunoassay; LPS: lipopolysaccharide.

## الانترليوكين ٦ اللعابي ودوره بتطور عملية التهاب اللثة

**الخلاصة** انترليوكين ٦ جزيئات بروتين نشطه بيولوجيا تعرف باسم السيتوكينات . تتم عملية انتاج هذه السيتوكينات في كريات الدم البيضاء والخلايا الشحميه والخلايا البطانية وتتم انتاج السيتوكينات في العمليات الالتهابيه بشكل رئيسي.

هذا النوع من السيتوكين له دور في تحفيز الاستجابه المناعيه المصاحبه للعمليات الالتهابيه من خلال انتاج بروتينات المرحله الحاده التي تصاحب عمليه الالتهابات .

ان عمليه انتاج هذا السيتوكين تتم وفقا للشفره التي ينقلها الرنا النقل من النواة وتكون عملية الانتاج في حالة زيادة او نقصان وفقا لحالة اللثة في حالة الالتهاب او الصحه أي ان مستوى هذا السيتوكين يعكس عمليه التهاب اللثة ويكون تحت سيطرة من النواة .

الكلمات الرئيسية: اللعاب ، انترليوكين ٦ ، التهاب اللثة