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### Original Article

## Evaluation of IL-6 levels in Patient with Chronic Generalized Periodontitis : A Case Control Study

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#### ABSTRACT:

**Background:** Chronic periodontitis is an inflammatory disease affecting the supporting tissues of teeth. The expression of the disease results from the interaction of host defense mechanisms, microbial agents, environmental, and genetic factors. **Aim of the study:** To evaluate IL-6 level in patient with chronic generalised periodontitis. **Materials and methods:** The study was conducted in the Department of Periodontology of the medical institution. For the study, we selected 30 patients with chronic periodontitis and 30 control subjects. A sample of gingival was surgically removed from the patients for the estimation of IL-6 in the gingival tissue. The estimation of IL-6 for each patient was done using ELISA method following the manufacturer's instructions. The level of IL-6 for each patient was noted and was subjected to statistical analysis. **Results:** A total of 30 patients were enrolled in each group, Chronic periodontitis group and Control group. The mean age of patients in periodontitis group was 34.56 years and in control group was 33.45 years. Mean IL-6 level in periodontitis group was 28.12 pg/mL and in control group was 15.92 pg/mL. **Conclusion:** From the results of present study, this can be concluded that patients with chronic generalized periodontitis tend to have elevated level of IL-6. These salivary biomarkers are likely to provide great clinical benefit when supplemented with other clinical information.

**Keywords:** Periodontitis, IL-6, gingivitis.

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#### INTRODUCTION:

Chronic periodontitis is an inflammatory disease affecting the supporting tissues of teeth. The expression of the disease results from the interaction of host defense mechanisms, microbial agents, environmental, and genetic factors.<sup>1,2</sup> Various compounds, such as cytokines, have been detected in gingival crevicular fluid (GCF) and may be especially beneficial for diagnosing current periodontal status and addressing the effects of periodontal treatment.<sup>3</sup> Cytokines namely interleukin (IL) -6, IL-1 and tumor necrosis factor- $\alpha$  play important role in the immunopathology of periodontal disease. Thus, the genetic regulation of cytokine function may influence the severity

of periodontitis.<sup>4</sup> Different types of cells secrete IL-6 and its level of secretion are influenced by the type of cell, type of stimulant, and the underlying genetic mechanism. IL-6 is an important inflammatory mediator and has both pro- and anti-inflammatory properties.<sup>5</sup> Single-nucleotide gene polymorphisms of -572 G/C and -174 G/C which are common polymorphisms in the IL-6 gene promoter affect the expression of IL-6 and increase its serum level causing its higher transcription and consequently greater induced response. Increased IL-6 serum level is correlated with inflammatory diseases like periodontitis.<sup>6</sup> Hence, the present study was conducted to evaluate IL-6 level in patient with chronic generalised periodontitis.

**MATERIALS AND METHODS:**

The study was conducted in the Department of Periodontology of the medical institution. The ethical clearance for study protocol was obtained from ethical committee of the institution. For the study, we selected 30 patients with chronic periodontitis and 30 control subjects. A sample of gingival was surgically removed from the patients for the estimation of IL-6 in the gingival tissue. The estimation of IL-6 for each patient was done using ELISA method following the manufacturer’s instructions. The level of IL-6 for each patient was noted and was subjected to statistical analysis.

The statistical analysis of the data was done using SPSS version 11.0 for windows. Chi-square and Student’s t-test were used for checking the significance of the data. A p-

value of 0.05 and lesser was defined to be statistical significant.

**RESULTS:**

Table 1 shows the demographic details of the participants. A total of 30 patients were enrolled in each group, Chronic periodontitis group and Control group. The mean age of patients in periodontitis group was 34.56 years and in control group was 33.45 years. Number of male subjects in periodontitis group was 31 and in control subjects was 29. Table 2 shows mean IL-6 level in both groups. Mean IL-6 level in periodontitis group was 28.12 pg/mL and in control group was 15.92 pg/mL. The results were compared and were found to be statistical significant.

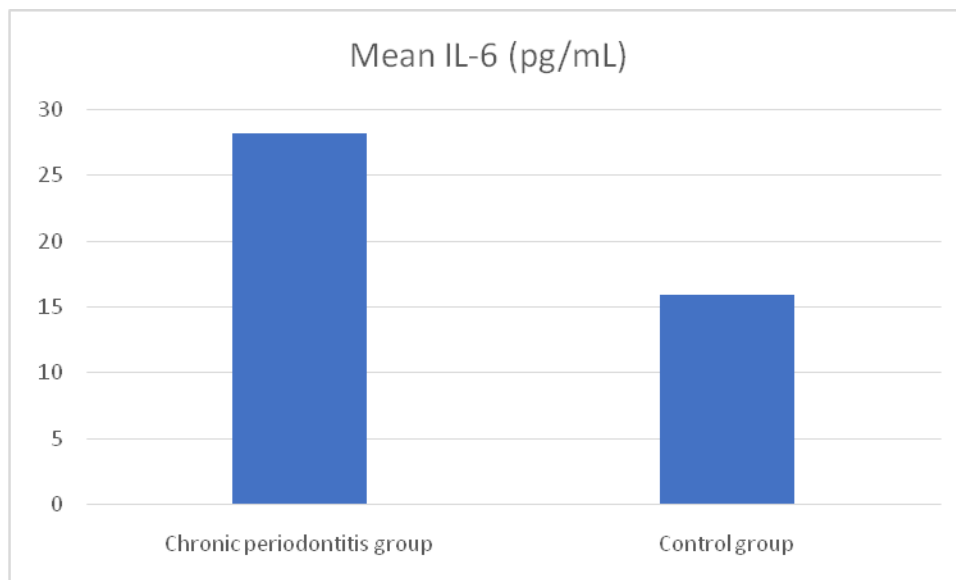
**Table 1: Demographic details of patients in both groups**

Variables	Chronic periodontitis group	Control group
Mean age (years)	34.56	33.45
Number of patients	30	30
Number of male subjects	31	29
Number of female subjects	19	21

**Table 2: Mean IL-6 level in both groups**

Group	Mean IL-6 (pg/mL)	p-value
Chronic periodontitis group	28.12	0.002
Control group	15.92	

**Figure 1: Mean IL-6 level in both groups**



**DISCUSSION:**

In the present study, a total of 30 patients were enrolled in each group, Chronic periodontitis group and Control group. We observed significant elevated IL-6 level in chronic periodontitis group as compared to control subjects. The results were compared with previous studies. Machado V et al characterized the salivary levels of two inflammatory biomarkers associated with periodontitis, interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF- $\alpha$ ), in order to assess whether these cytokines salivary levels could potentially be used to complement periodontitis pregnant women diagnose. Forty-four pregnant women were distributed into three groups, according to their periodontal status: healthy, mild/moderate periodontitis and severe periodontitis. Unstimulated saliva was collected and analysis of TNF- $\alpha$  and IL-6 salivary levels were performed with Immulite®. Women with periodontitis exhibited significantly higher levels ( $p = 0.001$ ) of salivary IL-6 and TNF- $\alpha$  compared with the healthy group: 25.1 ( $\pm 11.2$ ) pg/mL vs. 16.3 ( $\pm 5.0$ ) pg/mL and 29.7 ( $\pm 17.2$ ) pg/mL vs. 16.2 ( $\pm 7.6$ ) pg/mL, approximately 1.5 and 1.8 times more, respectively. Additionally, cytokines were significantly increased in severe periodontitis compared to periodontal healthy pregnant women. These results revealed that IL-6 and TNF- $\alpha$  salivary biomarkers provide high discriminatory capacity for distinguishing periodontal disease from periodontal health in pregnant women. Shyu KG et al investigated the relationship between proinflammatory cytokines in saliva and periodontal status. To investigate the usefulness of cytokines in the therapeutic approach for periodontal disease, the relationship between stimulated cytokine changes and the periodontitis treatment outcome was investigated in this study. Saliva was obtained from 22 patients diagnosed by dentists as having chronic periodontitis. The proinflammatory cytokine (interleukin-1 $\alpha$  (IL-1 $\alpha$ ), interleukin-1 $\beta$  (IL-1 $\beta$ ), interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), and tumor necrosis factor  $\beta$  (TNF- $\beta$ )) levels were determined using a commercially available kit. The IL-1 $\beta$  and IL-6 levels increased, whereas the TNF- $\beta$  levels decreased with the severity of periodontitis (4 mm pocket percentage). Poststimulation IL-1 $\alpha$ , IL-6, and IL-8 levels were higher in patients who had an improved treatment outcome. The differences of IL-6 levels (cut point: 0.05  $\mu\text{g/g}$ ) yielded a sensitivity and specificity of 90.0% and 81.82%, respectively, for predicting the periodontitis treatment outcome. Among the proinflammatory cytokines, stimulated IL-6 was an excellent marker for predicting the periodontitis treatment outcome.<sup>7, 8</sup>

Noh MK et al quantified IL-6, IL-8 and TNF- $\alpha$  levels in the human gingival tissues of patients with periodontitis and to assess the correlation of these three cytokines with each other. In this study, human gingival tissues from 19 patients with periodontitis were collected. The tissues were homogenized, centrifuged and the protein in the supernatant was quantified. Enzyme-linked immunosorbent

assay (ELISA) was used in the measurement of the IL-6, IL-8 and TNF- $\alpha$  levels, and the mean levels were observed to be  $8.41 \pm 0.25$ ,  $34.01 \pm 1.09$  and  $20.70 \pm 0.31$  pg/ml, respectively. The mean levels of IL-8 were higher than those of the other two cytokines. In each sample, the level of TNF- $\alpha$  expression was consistently high, with little difference between the results, which contrasted with the fluctuations in IL-6 and IL-8 levels. The expression of the two ILs (IL-6 and IL-8) showed a positive correlation, whereas TNF- $\alpha$  levels were not correlated with IL-6 or IL-8 levels. These results suggest that IL-6, IL-8 and TNF- $\alpha$  may be relevant in the pathophysiology of periodontitis, and the measurement of these cytokines may be beneficial in the identification of patients with periodontitis. Salman BN et al assessed the correlation of interleukin 6 (IL-6) -174-GC and IL-6-572-GC gene polymorphisms with periodontal disease in an Iranian population. This case-control analytical study was conducted on 129 subjects presenting to the laboratory of Taleghani Hospital. Subjects underwent clinical and periodontal examinations and divided into five groups of healthy, gingivitis and mild, moderate and severe periodontitis. Blood samples (2 ml) were obtained. Genomic DNA was extracted manually using the salting-out method. IL-6 sequence amplification was performed using polymerase chain reaction with three thermal protocols. Digested products were analyzed by electrophoresis through 2% agarose gel using Gel Red staining. Data were analyzed using Chi-square, Kruskal-Wallis, and Mann-Whitney tests, and  $P < 0.05$  was considered significant. The frequency of GG polymorphism at IL-6-174 and IL-6-572 genomic regions was 51.2% and 71.3%, respectively. The frequency of IL-6-572-GG polymorphism was significantly greater than that of IL-6-572-GC polymorphism. Comparison of the mean and maximum pocket depth and clinical attachment level, as well as bleeding on probing percentage, revealed significant differences between the healthy controls and periodontitis patients. The frequency percentages of GC and GG polymorphisms were almost equal in the healthy, gingivitis, and periodontitis groups. In other words, the frequency of the two polymorphisms was not significantly different between the health and disease states. This study found no association between IL-6-174 and IL-6-572 gene polymorphisms and periodontitis in the studied population.<sup>9, 10</sup>

**CONCLUSION:**

From the results of present study, this can be concluded that patients with chronic generalized periodontitis tend to have elevated level of IL-6. These salivary biomarkers are likely to provide great clinical benefit when supplemented with other clinical information.

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