High Levels of Tumor Necrosis Factor-Alpha and Interferon-Gamma in Patients with Gingival Recession

Sura Dakhil Jassim1, Luma Jassim Witwit2, Fatima Malik Abood3
1MSc in Periodontology, College of Dentistry, Babylon University, 2MSc in Microbiology, College of Dentistry, Babylon University; 3PHD in Microbiology, College of Dentistry, Babylon University.

Abstract

Background: Gingival recession considers as a common condition that associated with transposition of the margin of the gingiva in to the position apical to the cemento-enamel junction which consequently result in an exposure of the root. Inflammatory biomarker including interferon-gamma and tumor necrosis factor-alpha associated with a significant role in periodontal tissue destruction. The main goals of current study were to compare the levels of interferon-gamma and tumor necrosis factor-alpha in patients with different degree of gingival recession and control participants.

Material and method: Blood samples taken from twenty four male participants and they grouped in to three groups as: group 1(8 control subjects), group 2 (8 patients with class 1 and 2 gingival recession) and group 3 (8 patients with class 3 and 4 gingival recession). Enzyme-linked Immunosorbent Assay was utilized to evaluate tumor necrosis factor-alpha and interferon-gamma levels.

Results: The levels of both biomarkers were greater in group 3 than group 1 and group 2 as well as group 2 had higher levels of these biomarkers than group 1.

Conclusion: Interferon-gamma and tumor necrosis factor-alpha could reflect periodontal destruction in patients with gingival recession.

Keywords: gingival recession, interferon-gamma, tumor necrosis factor-alpha and Enzyme-linked Immunosorbent Assays.

Introduction

The deposition of the gingival margin in an apical direction which consequently leads to revealing of the root surface to oral environment is called gingival recession (1). Periodontal disease, tooth malposition, trauma, aberrant frenal attachment strongly considered as etiological factors of gingival recession (2).

It is a very common condition, about 50% of persons in the populations have at least one or more sites of 1 mm of root exposure or more (3-5). Besides aesthetic shortcomings (6,7), gingival recessions have a high predisposition to be associated with functional problems related to root exposure, such as dentinal hypersensitivity (8-10), plaque retention, gingival inflammation, root caries (11-15), alveolar bone loss and eventually tooth loss (15, 16).

According to Miller (1985), 4 classes of gingival recessions were proposed. In class I the recession not includes mucogingival junction (MGJ), if the recession includes the MGJ the case considered as class II, both classes presenting no interproximal bone loss. In class III the recession extend to or include the MGJ with destruction of the interproximal bone and/or malpositioning of the tooth. Lastly, class IV presented with a severe destruction in the interdental bone and/or serious malpositioning of the tooth (17).

Proteins that are formed by different types of cells and represent a messenger to another cells are called
cytokines. They start, control and mediate inflammatory and immune reactions; as well they control differentiation and growth of cells\(^\text{18}\). Cells of gingival epithelium secrete a wide variety of cytokines, like, tumor necrosis factor-alpha (TNF-\(\alpha\)), interleukin-1a (IL-1a), interleukin-1b (IL-1b), interleukin-6 (IL-6) and interferon-gamma (IFN-\(\gamma\)) these are the pro-inflammatory cytokines while the anti-inflammatory cytokines include interleukin-10 (IL-10) and interleukin-4 (IL-4)\(^\text{19-21}\).

In chronic inflammation, cytokines like TNF, IFN, IL-1, and IL-6 perform a significant role in bone destruction by activating osteoclasts\(^\text{22-24}\).

**Material and Method**

A total twenty-four male subjects with age range (30-40) were included in present study. Patients presenting at least two buccal gingival recession were enrolled while control showing no gingival recession. The participant were categorized as control (group 1) and patient groups furthermore patients divided in to two groups according to Miller gingival recession classification\(^\text{17}\). The first group include class 1 and 2 gingival recession (group 2) while the second group include class 3 and 4 gingival recession (group 3).

All patients were signed a written informed consent to participate in present study. Periodontal measurements involving plaque (PI) and gingival (GI) indices were recorded for each patients\(^\text{25, 26}\).

**Exclusion criteria include:**

Patients with systemic diseases.

Patients with previous periodontal treatments or who take medication.

Tooth with restoration or crown involving cemento-enamel junction (CEJ).

Tooth with root abrasion at the CEJ.

Presence of periodontal pocket.

**Blood collection and storage:**

Blood were collected using sterile disposable syringes from each group. Clotting of the blood samples were gained by leaving the blood samples overnight at 4°C or for 2 hours at room temperature then centrifuge for 15 minutes at 1000×g. Supernatant were collected and stored at -20 °C, the assay was carried out during the first month after storage.

**Quantitative determination of cytokines:**

Quantitative determination of both biomarkers in serum of patients groups and control group using Sandwich- Enzyme-linked Immunosorbent Assays (ELISA) as in manufacture instructions (Elabscience Biotechnology Co., Ltd).

**Statistical analysis .**

Statistical analysis include mean and standard deviation (SD) also analysis of variance (ANOVA) test was utilized to estimate the differences among groups. \(P\) value less than 0.05 regarded as significant.

**Results**

Means of TNF were (17.48± 11.93), (52.76 ± 18.81), (72.27 ± 42.54) in control group, group 2 and 3 respectively with significant difference between groups (\(P=0.003\)) as shown in table 1 and figure 1. Regarding IFN-\(\gamma\) control group had the lowest mean (47.59 ± 29.33) while group 3 had the highest mean (280.08 ± 121.35) also there was a high significant difference among groups as shown in table 1 and figure 2.

The results of present study revealed that there were highly significant differences in plaque and gingival indices among groups (\(P<0.001\)) as shown in table 1.

**Table 1: Mean and standard deviation of plaque index, gingival index, TNF-\(\alpha\) and IFN-\(\gamma\) of all groups.**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 Mean ± SD</th>
<th>Group 2 Mean ± SD</th>
<th>Group 3 Mean ± SD</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI</td>
<td>0.34±0.10</td>
<td>1.56±0.26</td>
<td>1.75±0.24</td>
<td>0.000</td>
</tr>
<tr>
<td>GI</td>
<td>0.35±0.09</td>
<td>1.80±0.24</td>
<td>1.87±0.24</td>
<td>0.000</td>
</tr>
<tr>
<td>TNF-(\alpha)</td>
<td>17.48±11.93</td>
<td>52.76±18.81</td>
<td>72.27±42.54</td>
<td>0.003</td>
</tr>
<tr>
<td>IFN-(\gamma)</td>
<td>47.59±29.33</td>
<td>140.14±81.76</td>
<td>280.08±121.35</td>
<td>0.000</td>
</tr>
</tbody>
</table>
Gingival recession may occur in dentitions with otherwise healthy periodontium. About the significance of gingival inflammation and dental plaque in progression of gingival recession, other researches have revealed that the most common cause of gingival recession was gingival inflammation. They proposed that the breakdown of connective tissue caused by a localized inflammatory process. Gingival recession results from epithelial cells reproduction into the connective tissue which cause a collapsing of the epithelial surface (27,28). Current study showed that the patients with gingival recession in both groups had higher gingival and plaque indices than control group and these results were in concurrence with other studies who revealed that the gingival recession was related to the high levels of both dental plaque and calculus as well as it related to the gingival bleeding on probing (27,29-33). Also, a study conducted by Goutoudi et al. (34) shown that the gingival recession was concomitant with both high plaque scores and inflammation. One study (35) revealed a negative association between gingival recession and dental plaque.

The proinflammatory cytokine, TNF-α, induces the secretion of collagenase by the fibroblasts, bone and cartilage destruction. Tumor necrosis factor -α is part of the main proinflammatory cytokines which are usually produced on inflammatory sites by the mononuclear cells infiltration (36,37). In consequence, this cytokine is part of the periodontal tissue destruction. Previous studies reported an elevated levels of TNF-α in serum of periodontitis patients (38,39). Our results are corroborating with the previous data as we found great levels of TNF-α in serum of subjects with gingival recession (40).

Raised levels of numerous inflammatory mediators, like TNF-α, IFN-γ, IL-1, IL-6, and prostaglandinE2 (PGE2) have been identified in gingival crevicular fluid (GCF) and in gingival tissues of subjects presented with periodontal diseases (41,42).

The structure of bone tissue relies on the equilibrium between bone destruction and bone formation (43, 44). As key factors that contribute to the breakdown of periodontal tissue, several proinflammatory cytokines were identified, involving IL-1, TNF-α, IFN-γ, and IL-6 (45,46). It is possible that the higher levels TNF-α and IFN-γ found in our patients may have acted as an important osteoclastogenic factor by inducing the local osteoclast differentiation that could culminate in bone destruction.

Conclusion

Gingival recession presents an increase in inflammatory markers such as TNF-α and IFN-γ, which could be predictors of local bone destruction and disease spreading.

Ethical clearance: All participants received learned consent to join in current study, the study was accepted by Ethics team of Collage of Dentistry / Babylon University.

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Conflict of Interest: no conflict of interest in current study.

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