Changes of Salivary Interleukine-17, Apelin, Omentin and Vaspin Levels in Normal Subjects and Diabetic Patients with Chronic periodontitis

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Abstract

Background: Chronic periodontitis is a chronic inflammatory disease which is multifactorial. Diabetes mellitus is one of the major systemic factors to influence the severity of chronic periodontitis. Therefore, the aim of current study was to assess salivary biomarkers of Interleukine-17(IL-17), apelin, omentin and vaspin as putative candidates in the potential association between Diabetes mellitus and Chronic periodontitis. Methods: Whole saliva samples were collected from sixty adults sex and age-matched patients who were further divided into two groups; healthy (control group; n = 30) and diabetic individuals with chronic periodontitis (n = 30). Salivary IL-17, apelin, omentin and vaspin concentrations were determined by standard enzyme-linked immune-sorbent assay. Results: Salivary levels of IL-17, apelin and vaspin were significantly higher in diabetic patients with periodontitis group compared to control group. On the other hand, salivary levels of omentin were significantly lower in diabetic patients with periodontitis compared to control group. Conclusions: Our study supports the hypothesis that abnormal production of IL-17, apelin, omentin and vaspin can contribute to the pathogenesis of diabetes-related complications including Chronic periodontitis.

Keywords: Chronic periodontitis, omentin, apelin, IL-117, vaspin.

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Introduction

Periodontitis (PD) is a chronic inflammatory disorder mediated by host and bacterial interactions and manifested by damage to the periodontal tissues which may progress to tooth loss. Paradoxically the host reactions primarily intended to eliminate the invading bacteria responsible for the majority of the periodontal tissue destruction (¹). The pathogenesis of periodontitis involves the interaction between periodontal pathogens and host inflammatory and immune responses. Cytokines play a critical role in mediating inflammatory processes and tissue homeostasis underlying periodontitis. Diabetes mellitus (DM) is a metabolic disorder manifested by elevated levels of glucose in the blood and well-recognized as a risk factor for periodontal disease. Diabetic individuals present an increased prevalence, severity and progression of periodontitis when compared to non-diabetic subjects. Several mechanisms have been proposed to explain the biological link between DM and periodontal diseases including the formation of advanced glycation end products (AGEs), changes in collagen metabolism and immune
function, and an increased oxidative stress (2,3). There is a close relationship between DM and PD that has been well-acknowledged in many clinical and epidemiological studies (4,5).

Therefore, the objective of this study was to evaluate serum concentrations of Interleukine-17(IL-17), apelin, omentin and vaspin in diabetic patients with periodontitis compared to control group.

1. Materials and Methods

In current study, 60 patients were selected from clinic of Oral Medicine and Periodontology Department at Tikrit University/ College of Dentistry between April 2018 and February 2019. They were divided into two groups as follows: Group I: It included 30 patients suffering from diabetes with periodontitis.

Group II: It included 30 healthy subjects free from any systemic disease with healthy peridontium. Dental examination, clinical periodontal parameters, including plaque index (PI), gingival index (GI), probing pocket depth (PD), clinical attachment level (CAL) and bleeding on probing (BOP) were assessed (6), were conducted by well-trained dentist. Approximately 3ml of non-stimulated expectorated whole saliva was collected from each patient, into sterile tubes according to Navazesh method (7). Data were analyzed by SPSS 21. In addition, paired t-test and Pearson's correlation coefficient were employed to carry out coparisons. Statistical significance was defined at \( P<0.05 \).

Results   Descriptive statistics for both groups were illustrated in Table (1). The study conducted on group I (n=30) diabetic individuals with CP (9 females and 21 males) and group II (n=30) individuals without diabetes and periodontitis as control group (20 females and 10 males) the mean ±SD age in years was (40.3±3) and (38.6±4.2), respectively.

Biochemical findings

For omentin, there was a significant decrease in its salivary levels in diabetic patients with CP groups compared to controls \( (P<0.01; \) Table 1). In addition, IL-17, apelin and vaspin, their serum levels were significantly increased ( Table 2).

Table (1): Basic characteristics of study groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A (Controls)</th>
<th>Group B (Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>10/20</td>
<td>21/9</td>
</tr>
<tr>
<td>Age/years (mean±SD*)</td>
<td>38.6±4.2</td>
<td>40.3±3</td>
</tr>
</tbody>
</table>

*: Standard Deviation.
Table 2: Biochemical parameters of study groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Serum levels (mean±SD*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A (Controls)</td>
</tr>
<tr>
<td>Omentin (pg/mL)</td>
<td>57.90±4.76</td>
</tr>
<tr>
<td>IL-17 (pg/mL)</td>
<td>8.41±1.10</td>
</tr>
<tr>
<td>Apelin (pg/mL)</td>
<td>37.70±3.95</td>
</tr>
<tr>
<td>Vaspin (pg/mL)</td>
<td>0.6200±0.0876</td>
</tr>
</tbody>
</table>

*: Standard Deviation.

Figure 1: Correlation between Omentin and IL-17 in diabetics with periodontitis.
Figure 2: Correlation between Apelin and IL-17 in diabetics with periodontitis.

Figure 3: Correlation between Vaspin and IL-17 in diabetics with periodontitis.
2. Discussion

In this study, we sought to determine the levels of salivary Interleukine-17, apelin, omentin and vaspin levels in diabetic patients with CP. This study had two main findings; the first was that serum omentin levels were significantly lower in diabetic patients and the second was that serum IL-17, apelin and vaspin levels were significantly higher in diabetic patients with CP. The influence of DM on CP is well-accepted, whereby there is also substantial evidence indicating that diabetes is a risk factor for CP. Previous investigations demonstrated that chronic periodontitis severity is significantly associated with elevated plasma levels of many proinflammatory cytokines in individuals with Type 2 Diabetes Mellitus (T2D) (8). Apelin is a hormone that is synthesized by endothelial cells and exerts its functions through autocrine and paracrine pathways by binding to endogenous ligand of the G-protein coupled receptor expressed absolute presence in most types of cells in the heart, including myocytes, smooth muscle cells and fibroblasts. Apelin affects cardiovascular system and glucose homoeostasis (9,10). It is expressed by human adipocytes and up-regulated by insulin and obesity (11). Current study showed that the highest apelin concentrations were found in saliva from Group II. The mechanism resulting in higher salivary apelin levels in the CP groups remains unclear. It might be questioned whether salivary apelin is derived entirely from the circulation. However, mechanisms leading to acquisition and accumulation of apelin in saliva remain to be elucidated. As salivary flow rate was not measured in the present study, no judgment can be made on this point. Apelin may be released by many cell types in the oral cavity in response to bacterial activity. There is also a possibility that some other factors in the saliva of CP patients are capable of interfering with apelin assay, but this remains unknown as is IL-6 (12). Recently, periodontitis has been suggested to contribute to adipose tissue inflammation by promoting insulin resistance. Periodontitis are associated with insulin-resistance and insulin-induced apelin expression had been demonstrated in adipocytes. The presence and severity of periodontitis might influence salivary apelin and IL-6, originating from buccal adipocytes, may be involved in this response (4,13). IL-17 is a considered a proinflammatory cytokine produced by CD4 Th17 cells, which stimulate the production of proinflammatory mediators (14). In this study, the concentration of IL-17 was higher in GI, confirming the findings of (15) and (16) which might indicate a possible role of Th17 pattern in periodontitis when correlated to DM (17). This cytokine is associated with bone loss and with the production of other inflammatory markers such as IL-6, increasing the severity of periodontal inflammation. Vaspin a novel adipocytokine, visceral adipose tissue-derived serine protease inhibitor with insulin-sensitizing effects, may improve the metabolism of glucose, lipids and decrease glucose concentration (18) as well as plays inhibitory roles against inflammation in vascular smooth muscle (19). However, the overall impact of vaspin on glucose dysregulation in humans is not fully known. Serum vaspin levels in patients were higher in those in healthy controls. The notable dissimilarities in levels of vaspin might be explained by the presence of a systemic inflammatory condition. Omentin is a novel fat depot-specific secretary factor, an adipokine that is preferentially produced by visceral stromal adipose tissue. In vitro, omentin-1 increases insulin signal transduction by activating protein kinase B and enhances insulin-mediated glucose transport into adipocytes (20,21). The reduced level of Omentin might cause a reduction of insulin-induced glucose uptake by visceral and subcutaneous adipocytes or additional insulin-sensitive tissues and contributing, at least partially, to insulin resistance. Insulin and inflammation are closely linked, as such; omentin levels are likely linked to inflammation. These findings allow us to advocate that IL-17, apelin, omentin and vaspin levels might indicate chronic inflammation and that periodontitis may impact IL-17, apelin, omentin and vaspin release in DM patients. They also indicated that vaspin probably plays an important pro-inflammatory role. However, omentin might also play an important anti-inflammatory role in DM patients. This research was the first of its kind; however, it involved a fairly small sample size and was carried out over a short time frame. Future research will need to recruit more subjects and to take into account the increase in IL-17, apelin and vaspin levels and the reduction in omentin levels as hazard-based variables of periodontal disease and DM.
Conclusion

Our study supports the hypothesis that abnormal production of IL-17, apelin, omentin and vaspin can contribute to the pathogenesis of diabetes-related complications including chronic periodontitis.

Ethical Clearance: The research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq.

Conflict of interest: The authors declare that they have no conflict of interest.

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