Introduction

Chronic periodontitis and periimplantitis are inflammatory diseases resulting in irreversible loss of connective tissue and alveolar bone destruction. Leaving them untreated, tooth loss and implant failure may occur. Periodontitis is one of the most prevalent diseases affecting more than 50% of the adult population and...
its severe forms affect 11% of adults.

The increased demand for dental implants have resulted in an increase in the incidence of peri-implant diseases. The recent concern of individuals and practitioners is the 22% prevalence of periimplantitis, which is in need of greater attention.1

Early detection of diseases with an emphasis on screening patients, as well as professional interventions, help prevent complications, improve treatment and control diseases.2

Identifying biomarkers related to inflammatory conditions may help determine the presence, risk and progression of periodontal diseases such as periodontitis and periimplantitis, and it may help transform biomarker technology from the laboratory to chariside activities.3 Inflammatory biomarkers can easily be assessed in saliva. Therefore, saliva samples provide a non-invasive diagnostic test to evaluate periodontal diseases.4 Some studies have reported the measurement of cytokines and biomarkers in inflammatory disorders, especially the relevant biomarkers of periodontitis, including adiponectin, resistin, leptin, visfatin, tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6).5

Visfatin, originally named as pre-B-cell colony-enhancing factor and nicotinamide phosphoribosyl transferase, is a protein synthesized and secreted from adipose tissues and several cell types, including lymphocytes, bone marrow cells, hepatic cells, skeletal muscles, trophoblasts, and fetal membranes.6 This biomarker acts as a growth factor, cytokine, and enzyme and also induces destructive cytokines (IL-1β, TNF-α, and IL-6) in response to infection and inflammation.7

Few studies have evaluated gingival crevicular fluid (GCF) and serum levels of visfatin in periodontal diseases as in other inflammatory disorders. It has been demonstrated that visfatin levels positively correlated with the severity of periodontal disease.8-13 Salivary levels of visfatin also increase in patients suffering from periodontal inflammatory diseases as well.14-16

The aim of this study was to compare the salivary visfatin concentrations in patients with periimplantitis, periodontitis and healthy controls.

Methods
This case-control cross-sectional study was performed from March 2014 to March 2015. Patients visited with suspected periodontitis and patients who had received dental implants in the Department of Periodontics, Dental School, Shahid Beheshti University of Medical Sciences, were recalled and com-
of ≥5 mm in at least one measurement with bleeding on probing and/or suppuration. There had to be radiographic observation of crestal bone loss in at least one site around the implant. At least 2 threads of implants had to be exposed due to crestal bone loss. Implant success index (ISI) ratings of VI, VI, I and VIII were included in this study (Table 1).  

(SL: soft tissue level, HL: hard tissue level, PPD: probing pocket depth, BOP: bleeding on probing, RBL: radiographic bone loss detected via long cone parallel peri-apical technique, +: tissue level located at or coronal to the reference line, -: level apical to the reference line).  

Patients with no history of periodontitis and clinical attachment loss, BI<0.1 and PPD ≤3 mm in all sites were considered as the healthy group.  

**Biomarker Analysis**  
Each saliva sample (500 μL) was pipetted into a clean microcap tube and clarified by centrifugation at 10,000 g for 5 minutes. The supernatant was transferred to clean microcap tubes and used immediately for an enzyme-linked immunosorbent assay (ELISA). Concentrations of visfatin were determined using Human Visfatin (VISFATIN) ELISA Kit, according to the manufacturer’s instructions. The results of visfatin assay were expressed as ng/mL for concentrations. All the laboratory tests were performed in the Biology Department of Shahid Beheshti University of Medical Sciences (Bioassay Technology Laboratory, Shanghai, China).  

**Statistical Analysis**  
Statistical analyses were performed using SPSS 18. Comparisons of visfatin levels between the groups were performed with Kruskal-Wallis test. P-value < 0.05 was considered statistically significant.  

**Results**  
A total of 40 participants (21 females and 19 males) were enrolled in this study. They consisted of 16 patients with chronic periodontitis (8 females and 8 males/mean age: 38.12 years), 12 patients with periimplantitis (7 females and 5 males/mean age: 47.91 years) and 12 healthy individuals (6 females and 6 males/mean age: 35.08 years). The mean salivary visfatin concentrations in the periodontally healthy individuals, periimplantitis patients and chronic periodontitis patients were 23.97, 12.83 and 11.95 ng/mL, respectively (Table 2). However, visfatin levels were higher in the healthy individuals compared to other groups (Figure 1).  

No significant differences were found between salivary visfatin concentrations between the three groups (P=0.12).  

**Discussion**  
Various inflammatory biomarkers can be detected in both saliva and GCF. While GCF sampling is somehow invasive, collection of saliva can be used for convenient diagnosis of oral diseases.  

Visfatin, an inflammatory mediator which plays a role in increasing the secretion of TNF-α and IL-6 in monocytes, has been demonstrated to be increased by IL-1β in chondrocytes; consequently, the result is an increase in paracrine/autocrine function, which would lead to higher levels of prostaglandin E2.  

It has also been demonstrated that visfatin levels of serum increases in patients with chronic kidney disease, chronic obstructive pulmonary disease, Behçet’s syndrome, appendicitis, metabolic syn-

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**Table 1. Implant success index (ISI)**  

<table>
<thead>
<tr>
<th>Score</th>
<th>SL</th>
<th>HL</th>
<th>Clinical finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISI I</td>
<td>SL+, PPD≤4mm, BOP-</td>
<td>HL+</td>
<td>Clinically healthy</td>
</tr>
<tr>
<td>ISI II</td>
<td>SL+, PPD≤4mm, BOP+</td>
<td>HL+</td>
<td>Soft tissue information</td>
</tr>
<tr>
<td>ISI III</td>
<td>SL+, PPD&gt;4mm, BOP+</td>
<td>HL+</td>
<td>Deep soft tissue pocket</td>
</tr>
<tr>
<td>ISI IV</td>
<td>SL-</td>
<td>HL-, RBL≤2mm(≤20%)</td>
<td>Initiation of hard tissue breakdown</td>
</tr>
<tr>
<td>ISI V</td>
<td>SL-</td>
<td>HL-</td>
<td>Hard tissue breakdown plus</td>
</tr>
<tr>
<td>ISI VI</td>
<td>SL-</td>
<td>HL-, RBL: 2-4mm(40%)</td>
<td>Soft tissue recession</td>
</tr>
<tr>
<td>ISI VII</td>
<td>SL-</td>
<td>HL-, RBL: 2-4mm(40%)</td>
<td>Notable hard tissue breakdown</td>
</tr>
<tr>
<td>ISI VIII</td>
<td>-</td>
<td>RBL≥40%</td>
<td>Severe bone loss</td>
</tr>
<tr>
<td>ISI IX</td>
<td>-</td>
<td>Clinical mobility</td>
<td>Clinical failure</td>
</tr>
</tbody>
</table>

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**Table 2. The diffusion index of salivary visfatin level in patients with peri implantitis, periodontitis and healthy group**  

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Mean (ng/mL)</th>
<th>Med (ng/mL)</th>
<th>Min (ng/mL)</th>
<th>Max (ng/mL)</th>
<th>SEM (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periimplantitis</td>
<td>12</td>
<td>12.83</td>
<td>12.78</td>
<td>0</td>
<td>26.45</td>
<td>3.21</td>
</tr>
<tr>
<td>Periodontitis</td>
<td>16</td>
<td>11.95</td>
<td>0</td>
<td>0</td>
<td>33.66</td>
<td>3.57</td>
</tr>
<tr>
<td>Healthy</td>
<td>12</td>
<td>23.97</td>
<td>19.83</td>
<td>8.77</td>
<td>43.61</td>
<td>2.99</td>
</tr>
</tbody>
</table>
drome, inflammatory bowel disease and rheumatoid arthritis.\textsuperscript{7,26-31}

In periodontitis, visfatin is responsible for inflammatory reactions in periodontal structures and the consequent bone loss. It has been shown that microbial infection (presence of \textit{Fusobacterium nucleatum}) has a controlling influence on production of visfatin.\textsuperscript{32}

This study was designed to evaluate salivary visfatin concentrations in 40 age- and sex-matched patients with periimplantitis and periodontitis and periodontally healthy individuals. The results showed no significant differences in salivary visfatin levels between these three groups. In addition, in some of the samples related to periimplantitis and periodontitis groups, no visfatin was detected.

(PI: Periimplantitis; P: Periodontitis; G: Gingivitis; H: Healthy)

As shown in Table 3, our findings are contrary to those in other studies; probable reasons and limitations are listed below:

1. The small sample size, which is due to two main reasons:
2. This minimized the potential confounding factors and low incidence of periimplantitis
3. Presence of various standard classification systems approved for the diagnosis of disease.

Most studies consider a probing depth of \textgreater 5 mm, bleeding on probing with or without discharging pus and evidence of bone loss as criteria to determine periimplantitis.\textsuperscript{33} Probing depth alone is not an appropriate criterion and depends on factors such as the thickness of soft tissue, the depth of implant shoulders and the design of implant crest module. That's why we added it to the above criteria. Exposure of at least two threads of implant, which can be observed on radiograph, would provide a more accurate diagnosis of periimplantitis.

2. Different types of implants may be another reason for controversies in the results.
3. Different loading periods of implants
4. Difficulty of clinical diagnosis of initial gingivitis from healthy individuals. Therefore, a number of healthy people in the study might be in the early stages of gingivitis.
5. According to a study by Mamali et al, measurement of visfatin in saliva might not be reliable; therefore, further studies are necessary in order to confirm whole saliva as a proper fluid for the evaluation of visfatin.\textsuperscript{34}

6. In this study, the time of collecting saliva samples differed from other studies. Not to interfere in induction of biomarkers, the sampling was conducted before measuring PPD and BOP.

Further studies are needed to evaluate the effects of the factors we excluded from the study. In order to consider salivary visfatin as an inflammatory biomarker of periodontitis, further longitudinal studies are necessary, using a larger sample size in different populations.

Table 3. Studies on the level of visfatin in periodontal diseases

<table>
<thead>
<tr>
<th>Studies on visfatin</th>
<th>Number of patients</th>
<th>Groups</th>
<th>Sample</th>
<th>Analysis by</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paradeep et al 2011</td>
<td>40</td>
<td>CP, G, H</td>
<td>GCF, Serum</td>
<td>ELISA</td>
<td>increased in GCF and serum with the severity of disease from healthy to gingivitis to periodontitis groups</td>
</tr>
<tr>
<td>Raghavendra et al 2012</td>
<td>30</td>
<td>CP, Treated CP, H</td>
<td>GCF, Serum</td>
<td>ELISA</td>
<td>decreased after non-surgical periodontal treatment</td>
</tr>
<tr>
<td>Paradeep et al 2012</td>
<td>30</td>
<td>DM+CP, CP, H</td>
<td>GCF, Serum</td>
<td>ELISA</td>
<td>increased in both serum and GCF in individuals with T2 DM with CP</td>
</tr>
<tr>
<td>Alizadeh Tabari et al 2013</td>
<td>40</td>
<td>CP, H</td>
<td>Saliva</td>
<td>ELISA</td>
<td>significantly higher in periodontitis group</td>
</tr>
<tr>
<td>Ozcan et al 2014</td>
<td>72</td>
<td>CP, G, H</td>
<td>Saliva</td>
<td>ELISA</td>
<td>higher in patients with gingivitis and periodontitis compared to healthy subjects. gingivitis = periodontitis</td>
</tr>
<tr>
<td>Alizadeh Tabari et al 2015</td>
<td>40</td>
<td>CP, Treated Saliva, CP, H</td>
<td>Saliva</td>
<td>ELISA</td>
<td>reduced after non-surgical periodontal therapy to the levels comparable with those found in healthy individuals.</td>
</tr>
<tr>
<td>Present study</td>
<td>40</td>
<td>PI, CP, H</td>
<td>Saliva</td>
<td>ELISA</td>
<td>higher in healthy individuals; no significant differences were found in between the three groups</td>
</tr>
</tbody>
</table>

Conclusion

Under the limitations of this study, no significant relationships were found in salivary concentrations of visfatin between periimplantitis and chronic peri-

Figure 1. Salivary visfatin levels (ng/mL) in patients with periimplantitis (PI), periodontitis (P) and healthy individuals (H).
References


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odontitis patients and healthy controls.

Competing interests
There is no conflict of interests in this work.

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