Periodontal Status and Whole Salivary Cytokine Profile Among Smokers and Never-Smokers With and Without Prediabetes

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Background: Whole salivary interleukin (IL)-1β and IL-6 in smokers and never-smokers with prediabetes remains uninvestigated. The aim of this study is to assess the periodontal status and whole salivary IL-1β and IL-6 levels among smokers and never-smokers with and without prediabetes (controls).

Methods: Ninety-five males (45 with prediabetes and 50 systemically healthy controls) were included. Twenty-seven controls and 29 patients with prediabetes were smokers. Periodontal parameters (plaque index, bleeding on probing, probing depth, clinical attachment loss, and marginal bone loss) were measured, and the number of missing teeth were recorded. Fasting blood glucose (FBG) and hemoglobin A1c (HbA1c) levels were recorded. Unstimulated whole saliva samples were collected, unstimulated whole salivary flow rate (UWSFR) was determined, and IL-1β and IL-6 levels were measured. P values <0.05 were considered statistically significant.

Results: FBG (P<0.05) and HbA1c (P<0.05) levels were higher among patients with prediabetes than controls. All patients with prediabetes were hyperglycemic. UWSFR was significantly higher among controls than among patients with prediabetes (P<0.05). Periodontal parameters and whole salivary IL-1β and IL-6 levels were comparable among smokers and never-smokers with prediabetes. Among controls, periodontal parameters and whole salivary IL-1β and IL-6 levels were higher among smokers than never-smokers (P<0.05).

Conclusions: Among controls, periodontal inflammation was worse, and whole salivary IL-1β and IL-6 levels are higher in smokers than never-smokers. Among patients with prediabetes, periodontal inflammation and whole salivary IL-1β and IL-6 levels were comparable between smokers and never-smokers.


KEY WORDS
Chronic periodontitis; interleukins; prediabetic state; saliva.

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Studies\(^1\)\(^-\)\(^4\) have reported that chronic periodontitis (CP) is a common manifestation in patients with impaired glucose tolerance (or prediabetes) than systemically healthy individuals (controls). There is a cascade of events that jeopardize the periodontal status in patients with hyperglycemia compared with controls.\(^5\) Persistent hyperglycemia in patients with prediabetes has been hypothesized to increase the formation and accumulation of advanced glycation end products (AGEs) in periodontal tissues, and interactions between AGEs and their receptors (RAGEs) play an essential role in augmenting periodontal inflammation.\(^6\) It has been reported that AGE–RAGE interactions induce increased cellular oxidative stress and stimulates the production of proinflammatory cytokines, such as interleukin (IL)-6, IL-1\(\beta\), and matrix metalloproteinases, that worsen the chronic inflammatory state and enhance bone loss.\(^7\)\(^,\)\(^8\) In addition, oxidative stress (induced by chronic hyperglycemia) imbalances the equilibrium between the production and the inactivation of reactive oxygen species (ROS), such as superoxide anion, hydroxyl radical, and peroxyl radical.\(^9\) The chronic existence of ROS promotes tissue damage and enhances cell death.\(^9\) Furthermore, an imbalance between periodontopathogens and the host response in patients with chronic hyperglycemia also enhances the expression of proinflammatory cytokines in saliva, serum, and gingival crevicular fluid and dysregulates the function of polymorphonuclear leukocytes (PMNs).\(^7\)\(^,\)\(^10\)\(^-\)\(^12\) These factors contribute to the breakdown of supporting connective tissue attachment and alveolar bone.

It is well-known that smoking is an independent and significant risk factor of CP.\(^13\)\(^,\)\(^14\) Studies\(^2\)\(^,\)\(^15\) have shown that plaque index (PI), probing depth (PD), and clinical attachment loss (AL) are worse in smokers compared with never-smokers. In addition, radiographic evidence has shown that marginal bone loss (MBL) is significantly higher in smokers compared with never-smokers.\(^15\) In addition, smoking masks the clinical signs of periodontal inflammation by suppressing bleeding on probing (BOP),\(^16\) thereby making patients unaware of their compromised periodontal health status and ongoing periodontal breakdown.

Unstimulated whole saliva (UWS) is a complex oral fluid that can be collected easily using non-invasive methods. Studies\(^17\)\(^-\)\(^19\) have shown that a variety of inflammatory biomarkers (such as IL-1\(\beta\), IL-6, and immunoglobulins [Igs]) are expressed in the UWS of patients with oral and systemic disorders.\(^17\)\(^,\)\(^18\)\(^,\)\(^20\)\(^,\)\(^21\) Therefore, assessment of UWS may yield valuable information and can be used for monitoring the severity of oral inflammatory conditions, including CP.\(^22\) IL-6 and IL-1\(\beta\) are inflammatory cytokines that enhance bone resorption by increasing osteoclastic activity\(^23\) and also mediate periodontal soft tissue breakdown through the stimulation of proteases.\(^23\)\(^-\)\(^25\)

Because CP is a common manifestation in habitual smokers and patients with prediabetes compared with systemically healthy controls and never-smokers, the following is hypothesized: 1) CP is worse in smokers with prediabetes compared with never-smokers with prediabetes and systemically healthy smokers and never-smokers; and 2) concentrations of IL-6 and IL-1\(\beta\) (UWS are higher among smokers with prediabetes and control smokers compared with never-smokers with prediabetes and control never-smokers.

The aim of the present study is to assess the periodontal status and whole salivary IL-1\(\beta\) and IL-6 levels among smokers and never-smokers with and without prediabetes.

**MATERIALS AND METHODS**

**Ethical Guidelines**

The study protocol was reviewed and approved by the research ethics review committee of Jinah Hospital, Karachi, Pakistan (OR-174-2012). Consenting individuals were requested to read and sign a consent form. It was mandatory for consenting individuals to have read and signed the consent form before being included in the present investigation.

**Inclusion and Exclusion Criteria**

Individuals with medically diagnosed prediabetes (fasting blood glucose levels [FBGLs] of 100 to 125 mg/dL [5.6 to 6.9 mmol/L] and levels of hemoglobin A1c [HbA1c] of 5.7% to 6.4%)\(^26\) and self-reported systemically healthy controls were included. Exclusion criteria comprised the following: 1) self-reported systemic diseases other than prediabetes, such as type 1 diabetes mellitus (DM) and type 2 DM, human immunodeficiency virus infection/AIDS, cardiovascular disorders, epilepsy, hepatic disorders, and renal disorders; 2) antibiotic and/or steroid intake within the past 3 months; 3) misaligned teeth or patients requiring orthodontic therapy because malocclusion itself is a potential cause of plaque stagnation on teeth surfaces; 4) edentulism; 5) self-reported habitual tobacco chewing and alcohol consumption; 6) history of periodontal treatment within 6 months; 7) pregnancy; and 8) non-smokers who had a previous history of smoking.

**Study Design and Participants**

The present convenience sample case-control study was performed from August 2012 to July 2013. Patients with prediabetes were recruited from the diabetes care unit of a local hospital in Karachi, Pakistan. Controls were recruited from the Section of Dentistry of the local hospital in Karachi, Pakistan. All patients were examined at the Section of Dentistry of the same hospital (as stated above). Individuals who reported smoking at least one cigarette daily for at least 1 year were defined as “smokers.” Individuals
who reported to have never consumed tobacco in any form were defined as “never-smokers.”

In the present study, 95 males (aged 36 to 55 years; mean age: 43.1 years) were included. Of the 95 patients, 45 patients (aged 40 to 45 years; mean age: 42.6 years) had prediabetes and 50 patients (aged 42 to 47 years; mean age: 44.5 years) served as controls. Twenty-nine patients with prediabetes and 27 controls were smokers. Individuals with prediabetes were requested to present their medical records to confirm the diagnosis of prediabetes. Among all individuals with prediabetes, prediabetes had been diagnosed in accordance with the criteria proposed by the American Diabetes Association.26

Periodontal examination and collection of UWS samples were performed at early morning hours. All participants were requested to visit the oral healthcare center in a fasting state.

**Collection of UWS Samples**

UWS samples were collected as described previously.27 In summary, participants were seated comfortably on a chair in a quiet room with their heads slightly bent forward. Saliva was allowed to accumulate in the patients’ mouth (without any stimulation) for 5 minutes, after which they were instructed to expectorate into a funnel connected to a gauged measuring cylinder. The patients were instructed to refrain from swallowing and moving the lips and tongue during saliva collection. Unstimulated whole saliva flow rate (UWSFR) was recorded in milliliters per minute. Immediately after collection, UWS samples were transferred immediately to disposable centrifuge tubes and placed on ice. UWS samples were aliquoted and frozen at –80°C. All UWS samples were analyzed within 6 months of collection.

**Measurement of IL-1β and IL-6 Levels in UWS**

UWS levels of IL-1β and IL-6 were investigated in duplicates using enzyme-linked immunosorbent assay. Human IL-6 kits** and IL-1β kits†† were used according to the instructions of the manufacturers. In summary, a standard curve was constructed using standards provided with the IL-6 and IL-1β kits, and protein concentrations were calculated from the standard curve. A total of 100 μL diluted standards with samples were dispensed, in duplicate, into the wells coated with a specific protein antibody. The plates were incubated at room temperature for 60 minutes, after which they were washed three times with a wash solution. One hundred microliters of conjugate solution was added, and the plates were incubated at room temperature for another 120 minutes. The wells were washed once again three times with a wash solution, and 100 μL substrate solution was added. The plates were incubated for 20 minutes at room temperature, after which 50 μL stop solution was added to terminate color development. Absorbance was determined by reading the plate at 450 nm in a spectrophotometer.

**Measurement of FBGLs and HbA1c Levels**

In all patients, the FBGL was measured using a digital glucometer‡‡ and expressed in milligrams per deciliters. HbA1c levels were investigated using ion-exchange high-performance liquid chromatography and expressed as percentages.

**Clinical Periodontal Examination**

Clinical periodontal examination was performed by a trained and calibrated investigator (FV) masked to the groups. The overall κ value for intraexaminer reliability was 0.78. Full-mouth PI,28 BOP,29 PD,30 and AL31 were measured at six sites per tooth (mesiobuccal, mid-buccal, disto-buccal, disto-lingual/palatal, mid-lingual/palatal, and mesio-lingual/palatal) on all maxillary and mandibular teeth (excluding third molars). The PD was measured to the nearest millimeter using a graded probe. §§ Fractured teeth with embedded root remnants were excluded.

**MBL**

Panoramic radiographs were taken using a digital panoramic tomography machine∥∥ and viewed on a calibrated computer screen¶¶ using a software program. **‡‡ MBL was measured as the vertical distance from 2 mm below the cemento-enamel junction (CEJ) to the most apical part of the marginal bone.15 MBL was measured on bilateral maxillary and mandibular premolars and molars (excluding third molars in both arches) by one investigator (FV). Tooth surfaces in which the CEJ and/or the bone crest were not clearly visible because of technical reasons (such as dental restorations, interdental caries, overlapping of teeth, and/or poor radiographic quality) were not sought.

**Statistical Analyses**

Statistical analyses were performed using a software program.*** Clinical parameters and salivary cytokine concentrations were assessed using one-way analysis of variance. The same software program was used to perform logistic regression analysis to evaluate the associations between smoking and prediabetes (after adjustment for age, smoking, and education status) with reference to periodontal parameters and whole salivary cytokine profile. For multiple logistic regression analysis, patients’ age, education status, and smoking were considered as confounders. For
multiple comparisons, Bonferroni post hoc adjustment test was used. Power and sample sizes were calculated using statistical software. With inclusion of at least 45 patients per group (assuming a standard deviation of 1.0%), the study power was estimated to be 80% to detect an association between periodontal status and whole salivary cytokine profile among smokers and never-smokers with and without prediabetes (with a two-sided significance level of 0.05). \( P \) values < 0.05 were considered statistically significant.

**RESULTS**

**Characteristics of the Study Population**

The mean ages of smokers and never-smokers with and without prediabetes were comparable (age range: 36 to 55 years). University graduate-level education status was significantly higher among controls \( (P < 0.01) \) compared with patients with prediabetes. The education of smokers \( (P < 0.05) \) and never-smokers \( (P < 0.05) \) in the control group was significantly higher than that among smokers and never-smokers with prediabetes. Among smokers and never-smokers with prediabetes, the duration of the prediabetic state was 12.5 ± 0.6 and 7.6 ± 2.1 months, respectively. A family history of diabetes was more often reported by patients with prediabetes \( (62.2\%) \) compared with controls \( (20\%) \). A family history of diabetes was comparable among smokers \( (68.9\%) \) and never-smokers \( (56.3\%) \) with prediabetes. (Table 1).

Duration of smoking was comparable among individuals with prediabetes and controls. Among controls, smokers smoked a significantly greater number of cigarettes on a daily basis compared with smokers with prediabetes \( (P < 0.01) \). A family history of smoking was reported by 68.9% of smokers with prediabetes and 25.9% of smokers in the control group (Table 1).

**FBGLs and HbA1c Levels**

FBGLs \( (P < 0.05) \) and HbA1c levels \( (P < 0.05) \) were significantly higher among patients with prediabetes.

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**Table 1.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Patients With Prediabetes</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Individuals ( (n = 45) )</td>
<td>Smokers ( (n = 29) )</td>
</tr>
<tr>
<td>Age (years; mean ± SD)</td>
<td>42.6 ± 3.2</td>
<td>40.5 ± 2.7</td>
</tr>
<tr>
<td>Males (n)</td>
<td>45</td>
<td>29</td>
</tr>
<tr>
<td>University graduate-level education status (%)</td>
<td>35.6*</td>
<td>31†</td>
</tr>
<tr>
<td>Duration of prediabetes (months; mean ± SD)</td>
<td>10.5 ± 1.2</td>
<td>12.5 ± 0.6</td>
</tr>
<tr>
<td>Family history of diabetes (%)</td>
<td>62.2</td>
<td>68.9</td>
</tr>
<tr>
<td>FBGL (mg/dL; mean ± SD)</td>
<td>118.4 ± 2.2§</td>
<td>120.5 ± 1.2†</td>
</tr>
<tr>
<td>Mean HbA1c (%; mean ± SD)</td>
<td>6 ± 0.2§</td>
<td>6.2 ± 0.1†</td>
</tr>
<tr>
<td>Treatment of prediabetes</td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>Allopathic only (%)</td>
<td></td>
<td>—</td>
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<tr>
<td>Dietary control only (%)</td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>Allopathic + dietary control (%)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Duration of smoking (years; mean ± SD)</td>
<td>18.3 ± 1.2</td>
<td>18.3 ± 1.2</td>
</tr>
<tr>
<td>Family history of smoking (%)</td>
<td>55.6</td>
<td>68.9</td>
</tr>
<tr>
<td>Cigarettes smoked daily (n; mean ± SD)</td>
<td>5.2 ± 3.3</td>
<td>5.2 ± 3.3¶</td>
</tr>
</tbody>
</table>

* \( P < 0.01 \), compared with all individuals in the control group.
† \( P < 0.05 \), compared with smokers in the control group.
‡ \( P < 0.05 \), compared with never-smokers in the control group.
§ \( P < 0.05 \), compared with all individuals in the control group.
¶ \( P < 0.01 \), compared with never-smokers in the control group.
††† nQuery Advisor v.6.0 software, Statistical Solutions, Saugus, MA.
Periodontal Inflammatory Conditions Among Smokers and Never-Smokers With Prediabetes and Controls

<table>
<thead>
<tr>
<th>Periodontal Parameters</th>
<th>Patients With Prediabetes</th>
<th>Controls</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>All Individuals (n = 45)</td>
<td>Smokers (n = 29)</td>
</tr>
<tr>
<td>PI (%)</td>
<td>70.5 ± 10.2*</td>
<td>75.3 ± 11.1†</td>
</tr>
<tr>
<td>BOP (%)</td>
<td>55.6 ± 7.8*</td>
<td>39.4 ± 10.1†</td>
</tr>
<tr>
<td>PD ≥4 mm (%)</td>
<td>45.7 ± 3.6*</td>
<td>49.3 ± 7.4†</td>
</tr>
<tr>
<td>AL (mm)</td>
<td>4.4 ± 0.5*</td>
<td>5.1 ± 0.2†</td>
</tr>
<tr>
<td>MBL (mm)</td>
<td>4.1 ± 1.1*</td>
<td>4.9 ± 1.2†</td>
</tr>
<tr>
<td>Missing teeth (n)</td>
<td>5.1 ± 2.3</td>
<td>5.9 ± 2.3</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD.
* P < 0.01, compared with all individuals in the control group.
† P < 0.05, compared with smokers in the control group.
‡ P < 0.01, compared with never-smokers in the control group.
§ P < 0.05, compared with never-smokers in the same group.

Periodontal Parameters Among Patients With Prediabetes and Controls After Controlling for Age, Smoking, and Education Status

<table>
<thead>
<tr>
<th>Periodontal Parameters</th>
<th>Patients With Prediabetes</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI (%)</td>
<td>61.4 ± 12.6*</td>
<td>29.14 ± 7.8</td>
</tr>
<tr>
<td>BOP (%)</td>
<td>49.7 ± 7.9*</td>
<td>25.8 ± 10.4</td>
</tr>
<tr>
<td>PD ≥4 mm (%)</td>
<td>38.5 ± 5.4*</td>
<td>8.4 ± 3.6</td>
</tr>
<tr>
<td>AL (mm)</td>
<td>3.4 ± 0.5*</td>
<td>0.6 ± 0.2</td>
</tr>
<tr>
<td>MBL (mm)</td>
<td>3.8 ± 0.6*</td>
<td>1.6 ± 0.2</td>
</tr>
<tr>
<td>Missing teeth (n)</td>
<td>4.2 ± 0.5</td>
<td>3.1 ± 0.3</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD.
* P < 0.01, compared with all individuals in the control group.

as compared with controls. FBGLs and HbA1c levels were comparable among smokers and never-smokers with prediabetes. All patients with prediabetes had been prescribed conventional hypoglycemic medicines and instructed to follow strict dietary control regimens by their health care providers.

Periodontal Inflammatory Parameters
Periodontal inflammatory conditions (PI, BOP, PD ≥4 mm, and AL) were worse among patients with prediabetes compared with controls (P < 0.01). PI, PD ≥4 mm, and AL were significantly higher among smokers with prediabetes compared with smokers in the control group (P < 0.05). There was no statistically significant difference in PI, BOP, PD ≥4 mm, and AL among smokers and never-smokers with prediabetes. Among control individuals, BOP was significantly lower in smokers compared with never-smokers (P < 0.05). PI, BOP, PD ≥4 mm, and AL were significantly higher in smokers with prediabetes compared with smokers in the control group (P < 0.05) (Table 2).

MBL was significantly higher among patients with prediabetes compared with controls (P < 0.01). MBL was significantly higher in smokers with prediabetes than smokers in the control group (P < 0.05). MBL was significantly higher in never-smokers with prediabetes compared with never-smokers in the control group (P < 0.01). There was no difference in MBL among smokers and never-smokers with prediabetes. Among controls, MBL was significantly higher in smokers than never-smokers (P < 0.05) (Table 2).

There was no statistically significant difference in the number of missing teeth among smokers and never-smokers with prediabetes and control smokers and never-smokers (Table 2). Multiple logistic regression analysis showed that PI, BOP, PD ≥4 mm, and AL remained significantly higher among patients with prediabetes than controls after adjustment for age, smoking, and education status (Table 3).

UWSFR
The UWSFR was significantly higher among controls compared with patients with prediabetes (P < 0.05). UWSFR was significantly higher in smokers in the control group compared with smokers with prediabetes.
**DISCUSSION**

The present study was based on the following hypotheses: 1) CP is worse in smokers with prediabetes than never-smokers with prediabetes and systemically healthy smokers and never-smokers; and 2) Concentrations of IL-6 and IL-1β UWS are higher among smokers with prediabetes and control smokers compared with never-smokers with prediabetes and control never-smokers. The results showed that clinical markers (PI, BOP, PD ≥4 mm, and AL), the radiographic parameter (MBL) of periodontal inflammation, and salivary IL-1β and IL-6 levels were comparable among smokers and never-smokers with prediabetes.

It is worth mentioning that all patients with prediabetes included in the present study were hyperglycemic despite the prescription of hypoglycemic medications and dietary control instructions by health care providers. This could possibly be associated with the education status, which was significantly higher among controls compared with those with prediabetes. It is likely that, because of poor education, patients with prediabetes remained unaware of the deleterious effects of hyperglycemia on oral and systemic health.

It has been reported that, in a chronic hyperglycemic state, interactions between AGEs and RAGEs are increased. This may impair the chemotactic and phagocytic function of PMNs and increase the production of proinflammatory cytokines (including IL-1β and IL-6). Moreover, results by Manouchehr-Pour et al. showed that chronic hyperglycemia impairs the chemotactic and phagocytic function of neutrophils (which prevent breakdown of bacteria in periodontal pockets), thereby increasing periodontal breakdown. Because smokers and never-smokers with prediabetes were hyperglycemic, it is speculated that the oxidative stress (induced as a result of hyperglycemia) worsened CP in these patients, thereby expressing comparable

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**Table 4.**

<table>
<thead>
<tr>
<th>Cytokines</th>
<th>Patients With Prediabetes</th>
<th>Controls</th>
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<tbody>
<tr>
<td>IL-1β (pg/mL)</td>
<td>147.5 ± 26.4*</td>
<td>151.4 ± 37.2†</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>125.5 ± 26.6*</td>
<td>136.7 ± 34.7†</td>
</tr>
</tbody>
</table>

* P<0.05, compared with all individuals in the control group.
† P<0.05, compared with smokers in the control group.
‡ P<0.01, compared with smokers in the control group.
§ P<0.01, compared with never-smokers in the same group.

**Table 5.**

<table>
<thead>
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</table>

* P<0.05, compared with all individuals in the control group.

(P<0.05). UWSFR was significantly higher in never-smokers in the control group than never-smokers with prediabetes (P<0.05). There was no statistically significant difference in UWSFR among smokers and never-smokers without and with prediabetes (Table 4).

**Whole Salivary IL-1β and IL-6 Levels**

Whole salivary IL-1β and IL-6 levels were significantly higher in patients with prediabetes compared with controls (P<0.05). Levels of IL-1β and IL-6 were significantly higher in smokers with prediabetes than smokers without prediabetes (P<0.05). Whole salivary IL-1β and IL-6 levels were significantly higher in never-smokers with prediabetes than smokers in the control group (P<0.01). There was no statistically significant difference in whole salivary IL-1β and IL-6 levels among smokers and never-smokers with prediabetes. Among controls, levels of IL-1β and IL-6 in UWS were significantly higher in smokers compared to never-smokers (Table 4). Multiple logistic regression analysis showed that UWS IL-1β and IL-6 remained significantly higher among patients with prediabetes than controls after adjustment for age, smoking, and education status (Table 5).
clinical (PI, BOP, PD ≥4 mm, and AL), radiographic (MBL), and immunologic markers (salivary IL-1β and IL-6) of periodontal inflammation in both groups, and the contribution of smoking in this regard was rather secondary.

Among controls, periodontal inflammatory parameters (PI, PD ≥4 mm, AL, and MBL) and whole salivary IL-1β and IL-6 were higher in smokers than never-smokers (Table 2). These results are in accordance with previous studies. The pathophysiologic mechanisms that augment periodontal breakdown in smokers compared with never-smokers include the following: 1) the expression of RAGEs in gingival tissues; 2) impaired functions of oral and systemic neutrophils and fibroblasts; 3) decreased production of IgA and IgG in saliva and serum; and 4) increased proliferation and prevalence of periodontopathogens. Moreover, habitual use of tobacco has also been shown to play a significant role in the elevation of periodontal inflammation whole salivary IL-6 and IL-1β levels. These mechanisms worsen CP in smokers compared with never-smokers.

The present results showed significantly lower BOP in smokers compared with never-smokers among controls. These results are in accordance with previous reports. An explanation in this regard can be derived from the hypothesis that nicotine in tobacco smoke minimizes gingival blood flow, thereby masking the clinical sign of gingival inflammation, which is BOP. However, it is noteworthy that, although smokers with prediabetes demonstrated numerically lower values for BOP compared with never-smokers in the same group, the comparison did not show a statistically significant difference (P = 0.09). Therefore, it is postulated that the high intensity of inflammation induced as a result of chronic hyperglycemia in patients with prediabetes empowered the vasoconstrictive effect of nicotine, thereby demonstrating comparable percentages of sites with BOP among never-smokers and smokers with prediabetes. In addition, another clarification that may be posed in this regard is that smokers with prediabetes were smoking significantly fewer cigarettes daily compared with controls. This factor may have also contributed to reducing the vasoconstrictive effect of nicotine in smokers with prediabetes compared with controls.

A limitation of the present study is that all participants were males. Studies have reported that multiple episodes of pregnancy, recurrent gestational diabetes, and obesity are significant risk factors of prediabetes among females. Therefore, it is hypothesized that CP is worse in females with prediabetes compared with males with prediabetes. In a recent study, showed that non-surgical periodontal therapy (NSPT) reduces hyperglycemia and periodontal inflammation in patients with prediabetes. It is speculated that NSPT and regular oral hygiene maintenance reduces hyperglycemia and the severity of CP in smokers and never-smokers with prediabetes; however, most favorable outcomes may be achieved via patient education, strict glycemic maintenance, and quitting the smoking habit. Moreover, it is pertinent to mention that there was an imbalance in the number of cigarettes smoked and duration of smoking among patients with prediabetes and controls. This factor could have biased the results reported in the present study. To rectify this discrepancy, additional studies with a larger sample size with comparable smoking habits among patients with prediabetes and controls are needed.

Furthermore, poor education is also a known risk factor of periodontal disease. In the present study, education status of controls was superior to that of patients with prediabetes. Therefore, it is tempting to speculate that the poor education status of patients with prediabetes may have played a role in aggravating periodontal inflammation in patients with prediabetes compared with controls. In the present study, all participants were informed about their oral hygiene status and were given instructions on how to maintain their systemic and oral health. In addition, all patients were offered free scaling and were also informed about the deleterious effects of smoking and hyperglycemia on overall health. Additional studies comparing periodontal status and whole salivary cytokine levels among smokers with prediabetes and control smokers (with comparable education status) are warranted to further elucidate the association between periodontal disease, prediabetes, and smoking habit.

CONCLUSIONS

It is concluded that, among controls, periodontal inflammation was worse and whole salivary IL-1β and IL-6 levels are higher in smokers than never-smokers. Among patients with prediabetes, periodontal inflammation and whole salivary IL-1β and IL-6 levels were comparable among smokers and never-smokers.

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REFERENCES


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