Periodontal Disease in Habitual Cigarette Smokers and Nonsmokers With and Without Prediabetes

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Abstract: Introduction: Prediabetes and habitual cigarette smoking are significant risk factors contributing to periodontal disease. The aim was to assess the clinical and radiological markers of periodontal disease in habitual cigarette smokers and nonsmokers with and without prediabetes. Methods: Sixty-eight individuals with prediabetes (test group; 34 smokers and 34 nonsmokers) and 68 medically healthy individuals (control group; 34 smokers and 34 nonsmokers) were included. Sociodemographic information, duration of smoking habit and number of cigarettes smoked daily were recorded through a questionnaire. Fasting blood glucose levels and periodontal inflammatory conditions (plaque index [PI], bleeding on probing [BOP] and probing pocket depth [PPD]) of 4 to <6 mm and ≥6 mm) were recorded. In both groups, marginal bone loss (MBL) was measured on digital panoramic radiographs. Results: Cigarette smokers and nonsmokers in the test group had significantly higher fasting blood glucose level when compared with cigarette smokers in the control group (P < 0.001). In the test group, there was no significant difference in PI, BOP, PPD (4 to <6 mm and ≥6 mm) and MBL among cigarette smokers and nonsmokers. Cigarette smokers in the control group had significantly higher PI (P < 0.001), PPD (4 to <6 mm; P < 0.001), PPD ≥6 mm (P < 0.01) and MBL (P < 0.05) than nonsmokers. BOP was significantly reduced in smokers when compared with nonsmokers in the control group (P < 0.001). Conclusions: Cigarette smokers without prediabetes exhibit significantly severe periodontal disease than nonsmokers. In subjects with prediabetes, the severity of periodontal disease seems to be over shadowed by the hyperglycemic state, obscuring the effect of habitual smoking.

Key Indexing Terms: Impaired glucose tolerance; Inflammation; Periodontal disease; Prediabetes; Smoking. [Am J Med Sci 2013;345(2):94–98]

The rapidly escalating global prevalence of diabetes implies a concomitant increase in the number of individuals with impaired glucose tolerance (IGT) or prediabetes worldwide. The prediabetes designations of impaired fasting glucose and IGT are defined by a fasting blood glucose level (FBGL) of 100 to 125 mg/dL and a postglucose challenge of 140 to 199 mg/dL, respectively. Although a number of studies have reported that periodontal inflammatory conditions are severe in patients with poorly controlled diabetes when compared with individuals with well-controlled diabetes and healthy individuals, little is known about the severity of periodontal disease in patients with prediabetes. Nearly, 2 decades ago, Sastrowijoto et al investigated the relationship between periodontal inflammatory parameters (gingival bleeding and dental plaque index [PI]) and IGT. They concluded that in individuals with IGT, the cumulative frequency and duration of increased blood glucose values may be too short to induce periodontal disease. In contrast, in an experimental study on Zucker rats, Pontes Andersen et al reported that prediabetes worsens periodontal inflammation. In a recent study, Javed et al also reported that the clinical (PI, bleeding on probing [BOP] and probing pocket depth [PPD 4 to <6 mm]) and radiological parameters of periodontal disease (marginal bone loss [MBL]) are aggravated in patients with prediabetes when compared with medically healthy individuals. The detrimental effects of cigarette smoking on oral and systemic health are well documented. Several studies have shown that habitual cigarette smokers are more susceptible to periodontal disease when compared with nonsmokers. It has been reported that tobacco smoking increases the expression of receptors of advanced glycation end products (AGEs) in gingival tissues and impairs the chemotactic and phagocytic functions of polymorphonuclear leukocytes. This in turn provokes a proinflammatory effect by stimulating the secretion of cytokines and reactive oxygen species which directly cause destruction of periodontal tissues. It is also noteworthy that gingival bleeding, a classic sign of periodontal inflammation, is masked in habitual smokers when compared with nonsmokers. Because of this, habitual smokers may be unaware of the periodontal destruction until the disease progresses to a stage where tooth mobility becomes evident.

Because prediabetes and habitual cigarette smoking are significant risk factors for periodontal disease, it is hypothesized that habitual cigarette smokers with prediabetes experience more intense periodontal disease when compared with habitual cigarette smokers without prediabetes. The aim of this study was to assess the clinical and radiological markers of periodontal disease in habitual cigarette smokers and nonsmokers with and without prediabetes.

MATERIALS AND METHODS

Study Participants

Individuals with medically diagnosed prediabetes (test group) were recruited from the Diabetes Care Unit of a hospital in Karachi, Pakistan; whereas subjects without prediabetes (control group) were recruited from a residential area located in the vicinity of the hospital. “Cigarette smokers” were defined as individuals who smoked at least 1 cigarette per day for a minimum of 12 months before the study period. “Non-smokers” were defined as individuals who reported to have never consumed tobacco in any form. The medical records from individuals in both groups were examined to ascertain the presence or absence of prediabetes.
In total, 136 individuals (68 individuals in the test group [34 smokers and 34 nonsmokers] and 68 individuals in the control group [34 smokers and 34 nonsmokers]) were recruited.

**Exclusion Criteria**

The exclusion criteria were as follows: (a) self-reported habitual alcohol and smokeless tobacco consumption; (b) edentulism; (c) individuals who self-reported to have other systemic disorders such as infection with human immunodeficiency virus disease, acquired immune deficiency syndrome, cardiovascular disorders, renal disease, hepatitis B and hepatitis C and (d) individuals currently using or those with a recent history of corticosteroid, antibiotic and/or nonsteroidal anti-inflammatory drug use.

**Interview Questionnaire**

In the test and control groups, information regarding age, gender, socioeconomic status, habitual cigarette smoking (yes/no), duration of smoking habit and number of cigarettes smoked daily was recorded through a questionnaire. Information regarding the treatment of prediabetes was also recorded.

**Measurement of FBGLs**

FBGLs in the test and control groups were measured by a digital glucometer (ACCU-CHEK ACTIV; Roche Diagnostics, Mannheim, Germany). The participants were categorized into 2 groups as follows: (a) healthy controls—individuals with FBGL <100 mg/dL (5.6 mmol/L) and (b) patients with prediabetes—individuals with FBGL of ≥100 mg/dL but <126 mg/dL (7.0 mmol/L).\(^{18}\)

**Clinical Periodontal Examination**

A single investigator, blinded to the prediabetic or the smoking status of individuals, performed all the clinical periodontal examinations. The overall kappa value for intraexaminer reliability was 0.78. A full-mouth PI, BOP and PPD (4 to <6 mm and ≥6 mm) were measured at 4 sites (mesial, distal, buccal and lingual/palatal) on all maxillary and mandibular teeth (excluding bilateral maxillary and mandibular third molars). PPD was measured to the nearest millimeters with a graded probe (Hu-Friedy Manufacturing, Chicago, IL).\(^2\) Fractured teeth with embedded root remnants were considered missing.

**Marginal Bone Loss**

Digital panoramic radiographs were taken using a digital panoramic tomography machine (KODAK 8000C System; Carestream Dental LLC, Atlanta, GA) and viewed on a calibrated computer screen (Samsung SyncMaster Digital TV Monitor, Korea) using a software program (Image Tool 3.0 Program; Department of Dental Diagnostic Science, University of Texas Health Science Center, San Antonio, TX). MBL was considered as the vertical distance from 2 mm below the cementoenamel junction to the most apical part of marginal bone.\(^2\) MBL was measured on bilateral maxillary and mandibular premolars and molars by a single investigator. Tooth surfaces at which the cementoenamel junction and/or the bone crest were not visible because of technical reasons (including dental restorations, interdental caries, overlapping of teeth and/or poor radiographic quality) and bilateral maxillary and mandibular third molars were excluded.

**Statistical Analysis**

The statistical analysis was performed using SPSS, Statistics 18.0, software program (Chicago, IL). One-way analysis of variance was used to determine whether the dependent variables (PI, BOP, PPD [4 to <6 mm and ≥6 mm], MBL and number of missing teeth) were statistically significant with the independent variables. The independent variables were transformed into dichotomous variables, for example, cigarette smokers in individuals with prediabetes, 1 versus nonsmokers in subjects with prediabetes, 0; cigarette smokers in individuals without prediabetes, 1 versus nonsmokers in individuals without prediabetes, 0. The Bonferroni adjustment post hoc test was performed for multiple comparisons. \(P\) values <0.05 were considered statistically significant. The power calculations performed before the study showed that the sample size required to ascertain the significance of association of periodontal disease in prediabetic smokers and nonsmokers with an alpha value of 0.05 and 85% power was 34 prediabetic smokers, 34 prediabetic nonsmokers, 34 smokers without prediabetes and 34 nonsmokers without prediabetes.

**Ethical Guidelines**

The study was approved by the research ethics review committee of the Engineer Abdullah Bugshan Research Chair for Growth Factors and Bone Regeneration, College of Dentistry, King Saud University, Riyadh, Saudi Arabia. Written consent was obtained from all individuals who agreed to participate in this study.

**RESULTS**

**Characteristics of the Study Population**

There was no significant difference in the mean age of cigarette smokers and nonsmokers in the test and control groups (Table 1). The mean duration of prediabetes among cigarette smokers and nonsmokers was 6.4 and 6.2 months, respectively. There was no significant difference in the duration of the smoking habit and the daily number of cigarettes per smoker among smokers in the test and control groups. These results are summarized in Table 1.

**Fasting Blood Glucose Levels**

The mean FBGL among individuals in the test group and control group were 120 mg/dL (range, 114-124 mg/dL) and 75.6 mg/dL (69-80 mg/dL) \((P < 0.001)\). In the test and control groups, there was no significant difference in FBGL among smokers and nonsmokers (Table 1). Cigarette smokers in the test group had significantly higher FBGL when compared with cigarette smokers in the control group \((P < 0.05)\). Nonsmokers in the test group had significantly higher FBGL when compared with cigarette smokers in the control group \((P < 0.01)\).

All patients with prediabetes were under a regimen of dietary control as prescribed by their physicians for the management of the metabolic state.

**Periodontal Inflammatory Conditions**

In the test group of prediabetics, there was no significant difference in PI, BOP, PPD (4 to <6 mm) and PPD (≥6 mm) among cigarette smokers and nonsmokers (Table 2).

Cigarette smoking prediabetics (test group) had a higher PI \((P < 0.001)\), BOP \((P < 0.001)\), PPD (4 to <6 mm; \(P < 0.001\)) and PPD (≥6 mm; \(P < 0.001\)) than cigarette smokers in the healthy control group. PI \((P < 0.001)\), BOP \((P < 0.001)\), PPD (4 to <6 mm; \(P < 0.001\)) and PPD (≥6 mm; \(P < 0.05\)) were also significantly higher among subjects in the test group compared with those in the control group (Table 2).

In the control group, cigarette smokers had significantly higher PI \((P < 0.001)\), PPD (4 to <6 mm; \(P < 0.001\))
and PPD (≥6 mm; P < 0.01) when compared with nonsmokers; however, BOP was significantly reduced in smokers when compared with nonsmokers in this group (P < 0.001).

**Marginal Bone Loss**

In the control group, MBL was significantly higher in smokers when compared with nonsmokers (P < 0.01). In the test group, there was no difference in MBL among smokers and nonsmokers. Nonsmokers in the test group showed significantly higher MBL when compared with smokers in the control group (P < 0.05). These results are shown in Figure 1

**DISCUSSION**

The present results demonstrate that in individuals without prediabetes, periodontal inflammatory conditions (PI, PPD [4 to <6 mm] and PPD [≥6 mm]) were significantly higher in smokers; however, gingival bleeding was reduced in smokers when compared with nonsmokers. Although these results are in agreement with previous studies\textsuperscript{2,10,11,19} that

**TABLE 1. Characteristics of the study population**

<table>
<thead>
<tr>
<th></th>
<th>Individuals with prediabetes (n = 68)</th>
<th>Individuals without prediabetes (n = 68)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cigarette Smokers (n = 34)</td>
<td>Nonsmokers (n = 34)</td>
</tr>
<tr>
<td>Age (yr; mean/range)</td>
<td>40.6/36-42</td>
<td>39.3/36-40</td>
</tr>
<tr>
<td>Gender</td>
<td>34 males</td>
<td>34 males</td>
</tr>
<tr>
<td>Duration of prediabetes (mo; mean/range)</td>
<td>6.4/3-8</td>
<td>6.2/3-7</td>
</tr>
<tr>
<td>FBGL (mg/dL; mean/range)</td>
<td>121.5/118-124</td>
<td>119.8/114-122</td>
</tr>
<tr>
<td>Duration of smoking habit (yr/range)</td>
<td>8.4/7-11</td>
<td>—</td>
</tr>
<tr>
<td>Number of cigarettes smoked daily (mean/range)</td>
<td>16.8/13-18</td>
<td>—</td>
</tr>
</tbody>
</table>

\( ^a P < 0.05. \)

\( ^b P < 0.01. \)

FBGL, fasting blood glucose level.

**TABLE 2. Clinical parameters of periodontal inflammation in habitual cigarette smokers and non-smokers with and without prediabetes**

<table>
<thead>
<tr>
<th>Parameters of periodontal inflammation</th>
<th>Individuals with prediabetes (n = 68)</th>
<th>Individuals without prediabetes (n = 68)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Smokers (n = 34)</td>
<td>Non-smokers (n = 34)</td>
</tr>
<tr>
<td>PI (%) (mean ± SD)</td>
<td>67.6\textsuperscript{a}</td>
<td>64.4\textsuperscript{a}</td>
</tr>
<tr>
<td>Range</td>
<td>45.8-85.9</td>
<td>50-89</td>
</tr>
<tr>
<td>BOP (%) (mean ± SD)</td>
<td>50.5\textsuperscript{a}</td>
<td>52.8\textsuperscript{a}</td>
</tr>
<tr>
<td>Range</td>
<td>23.1-77</td>
<td>39.6-70</td>
</tr>
<tr>
<td>PPD (4 mm &lt; 6 mm) (%)</td>
<td>28.7\textsuperscript{a}</td>
<td>29.3\textsuperscript{a}</td>
</tr>
<tr>
<td>Range</td>
<td>15.2-41.8</td>
<td>19.7-45</td>
</tr>
<tr>
<td>PPD (≥ 6 mm) (%)</td>
<td>12.2\textsuperscript{a}</td>
<td>11.5\textsuperscript{d}</td>
</tr>
<tr>
<td>Range</td>
<td>0-25.5</td>
<td>2.5-37.4</td>
</tr>
</tbody>
</table>

PI, Plaque index; BOP, Bleeding on probing; PPD, Probing pocket depth; mm, millimeters; SD, Standard deviation.

\( ^a P < 0.001. \)

\( ^b P < 0.01. \)

\( ^c P < 0.05. \)

\( ^d P < 0.01. \)

\( ^i \) indicates P < 0.05; \( ^j \) indicates P < 0.01.
assessed the effect of cigarette smoking on periodontal health, the exact mechanisms by which cigarette smoking increases periodontal inflammation remains poorly understood as yet. Various explanations have been proposed in this regard. Rezavandi et al.\(^{20}\) reported that the inflamed gingival tissues of smokers exhibit significantly smaller number of vessels when compared with nonsmokers. Similarly, Bergström et al.\(^{21}\) reported that the vascular reaction associated with plaque-induced gingivitis is suppressed in smokers when compared with nonsmokers. Smoking induces endothelial dysfunction that may lead to inflammatory activation within the vascular wall, mediated by cytokines (including interleukin [IL] 6, IL-8 and tumor necrosis factor-α) and adhesion molecules (particularly intercellular adhesion molecule-1).\(^{22}\) The level of soluble intercellular adhesion molecule-1 has been reported to be higher in smokers when compared with nonsmokers.\(^ {22}\) Serum concentrations of immunoglobulin G, mainly immunoglobulin G2 (an important antibody against gram-negative periodontal pathogens) are also decreased in smokers thereby making them more susceptible to develop periodontal disease when compared with nonsmokers.\(^ {23,24}\) According to the present results, there was no difference in BOP in smokers and nonsmokers with prediabetes. This suggests that the vasocconstrictive effect of nicotine does not mask gingival bleeding in prediabetic smokers and that there might be other mechanisms (such as increased accumulation of AGEs in periodontal tissues) that may play a role in augmenting BOP in smokers with prediabetes when compared with nonsmokers. It may therefore be suggested that increased gingival bleeding in smokers may be indicative of a “latent hyperglycemic state” in undiagnosed individuals. It is recommended that such individuals should be referred to physicians for medical assistance. Our results are in accordance with a recent study\(^ {25}\) in which the authors reported that oral healthcare professionals have the opportunity to identify undiagnosed diabetes and prediabetes in dental patients and refer them to a physician for further evaluation and care. However, further studies are warranted in this regard.

An interesting finding in this investigation was that the nonsmoking individuals in the test group showed significantly higher MBL when compared with cigarette smokers in the control group. It therefore seems that the intensity of periodontal inflammation induced by a hyperglycemic state (in patients with prediabetes) is more intense than the inflammatory response induced by cigarette smoking. Chronic hyperglycemia has been associated with an increased formation and accumulation of glucose-mediated AGEs in the gingival tissues, which in turn impairs the chemotactic and phagocytic function of polymorphonuclear leukocytes and produce proinflammatory cytokines, thereby leading to periodontal disease and MBL.\(^ {23}\) Although smoking has also been associated with an increased accumulation of AGEs in periodontal tissues, it is tempting to speculate that the amount of AGEs accumulation in hyperglycemic patients does not significantly impact upon the inflammatory condition of the periodontium, at least in the current cohort. This may perhaps explain the similarity in periodontal inflammatory parameters in prediabetic smokers and nonsmokers. Although the prediabetic individuals in the current cohort were recommended by their physicians to control hyperglycemia through dietary regimes both smokers and nonsmokers in this group had impaired fasting plasma glucose levels when compared with smokers and nonsmokers (without prediabetes).

It has been reported that increasing age, socioeconomic status, daily oral hygiene maintenance regimes and number of cigarettes smoked daily are directly associated with periodontal inflammation.\(^ {23,24}\) However, in this investigation, there was no significant difference in these variables among cigarette smokers and nonsmokers with and without prediabetes. This suggests that in this study, the severity of periodontal inflammation was mainly governed by hyperglycemia in prediabetic smokers and nonsmoker. Furthermore, studies on prediabetic smokers and nonsmokers with controlled glycemic statuses are warranted to assess the effect of cigarette smoking on periodontal health in these individuals.

**CONCLUSIONS**

In subjects without prediabetes, cigarette smokers had accentuated periodontal inflammation when compared with nonsmokers. In subjects with prediabetes, the severity of periodontal inflammatory parameters among smokers and nonsmokers was not significantly different implying that the hyperglycemic state may have obscured the adverse effect of habitual cigarette smoking on the periodontium.

**REFERENCES**


