Periodontal Inflammatory Conditions Among Smokers and Never-Smokers With and Without Type 2 Diabetes Mellitus

Fawad Javed,* Abdulaziz A. Al-Kheraif,† Karem Salazar-Lazo,* Virginia Yanez-Fontenla,* Khalid M. Aldosary,‡ Mohammed Alshehri,‡ Hans Malmstrom,* and Georgios E. Romanos§

Background: There is a dearth of studies regarding the influence of cigarette smoking on periodontal inflammatory conditions among patients with type 2 diabetes mellitus (T2DM). The aim of the present study is to assess periodontal inflammatory conditions among smokers and never-smokers with and without T2DM.

Methods: One hundred individuals (50 patients with T2DM [25 smokers and 25 never-smokers] and 50 controls [25 smokers and 25 never-smokers]) were included. Information regarding age, sex, duration and daily frequency of smoking, duration and treatment of diabetes, and oral hygiene was recorded using a questionnaire. Periodontal parameters (plaque index [PI], bleeding on probing [BOP], probing depth [PD], clinical attachment loss [AL], and marginal bone loss [MBL]) were measured. Hemoglobin A1c (HbA1c) levels were also recorded.

Results: Mean age, monthly income status, and education levels were comparable among smokers and never-smokers with and without T2DM. Mean HbA1c levels were significantly higher among patients with T2DM (8.2% ± 0.1%) compared with controls (4.4% ± 0.3%) (P <0.05). Smokers in the control group were smoking significantly greater numbers of cigarettes (15.5 ± 2.5 cigarettes daily) compared with smokers with T2DM (6.2 ± 2.1 cigarettes daily) (P <0.05). Periodontal parameters were comparable among smokers and never-smokers with T2DM. Among controls, periodontal parameters (PI [P <0.05], AL [P <0.05], PD ≥4 mm [P <0.05], and MBL [P <0.05]) were significantly higher in smokers than never-smokers. Never-smokers with T2DM had worse periodontal status than smokers and never-smokers in the control group (P <0.05).

Conclusions: Periodontal inflammatory conditions are comparable among smokers and never-smokers with T2DM. Among controls, periodontal inflammation is worse among smokers than never-smokers.


KEY WORDS
Alveolar bone loss; dental plaque; gingival bleeding on probing; inflammation; smoking; type 2 diabetes mellitus.
It is well established that chronic hyperglycemia is a significant risk factor for periodontal inflammatory conditions. Studies have shown that clinical parameters of periodontal inflammation (such as plaque index [PI], bleeding on probing [BOP], probing depth [PD] ≥4 mm, and clinical attachment loss [AL]) are worse among patients with poorly controlled type 2 diabetes mellitus (T2DM) compared with systemically healthy individuals (controls). Moreover, marginal bone loss (MBL) around teeth, a radiographic marker of periodontal inflammation, is also higher among patients with poorly controlled T2DM than controls. An explanation that has been given in this regard is that persistent hyperglycemia increases the formation and accumulation of advanced glycation end products (AGEs) in periodontal tissues, which in turn impair the chemotactic and phagocytic function of polymorphonuclear leukocytes and produce proinflammatory cytokines in the serum and gingival crevicular fluid. This leads to periodontal inflammation and MBL in patients with T2DM. Furthermore, the function of potential cells involved in immunoinflammatory responses is sabotaged in a chronic hyperglycemic state.

The deleterious effects of tobacco smoking on oral and systemic health are well documented. Habitual tobacco smoking has also been associated with an increased expression of receptors of AGEs in the gingival tissues. This in turn jeopardizes the chemotactic and phagocytic functions of polymorphonuclear leukocytes and provokes a pro-inflammatory effect by stimulating the secretion of cytokines and reactive oxygen species that directly cause breakdown of periodontal tissues. Clinical studies have also shown that habitual tobacco smokers exhibit greater numbers of sites with plaque accumulation, AL, and PD (≥4 mm) compared with individuals who never use tobacco in any form. It is important to mention, however, that BOP (a classic marker of periodontal disease activity) is masked in tobacco smokers. This most probably occurs as a result of the vasoconstrictive effect of nicotine on gingival blood vessels. Therefore, tobacco smokers may remain unaware of ongoing periodontal breakdown until the inflammatory process reaches a stage where tooth mobility becomes evident.

Because chronic hyperglycemia and habitual tobacco smoking are significant and independent risk factors of periodontal disease, it is hypothesized that periodontal inflammatory conditions are more intense among smokers with T2DM compared with never-smokers with T2DM. Therefore, the aim of the present study is to assess the periodontal inflammatory conditions among smokers and never-smokers with and without T2DM.

**MATERIALS AND METHODS**

**Ethical Guidelines**

The study was approved by the Research Ethics Review committee of the College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia (OR-114-2084). It was mandatory for all study participants to have read and signed the consent form before being included in the present investigation.

**Eligibility Criteria**

The inclusion criteria encompassed the following: 1) patients with medically diagnosed T2DM (hemoglobin A1c [HbA1c] ≥6.5%); 2) self-reported controls. The exclusion criteria were: 1) self-reported systemic diseases other than T2DM (such as human immunodeficiency virus infection/AIDS, cardiovascular disease, renal disease, hepatic disorders, and epilepsy); 2) edentulism; 3) crowding of teeth or occlusal trauma; 4) habitual alcohol use; 5) lactation and/or pregnancy; 6) use of antibiotics, non-steroidal anti-inflammatory drugs, and/or steroids within the past 3 months; or 7) bilateral maxillary and mandibular third molars.

**Study Participants and Groups**

From November 2013 to July 2014, a convenience sample case-control study involving smokers and never-smokers with and without T2DM was conducted at the College of Applied Medical Sciences, King Saud University. All participants were recruited from a local residential area in Riyadh, Saudi Arabia. In total, 100 males (50 patients with T2DM and 50 controls) were included. Clinical and radiographic examinations were performed at the College of Applied Medical Sciences, King Saud University. All participants who reported having T2DM were requested to present their medical records to verify the diagnosis of T2DM. Smokers were defined as individuals who reported smoking ≥1 cigarette daily for ≥1 year. Never-smokers were defined as individuals who reported never having consumed tobacco in any form.

**Questionnaire**

Information regarding sex, age, socioeconomic status (SES), education status (graduate level education: more than a 4-year college degree), duration of smoking, number of cigarettes smoked daily, duration of T2DM, treatment of T2DM recommended by health care provider, and daily oral hygiene maintenance protocols were collected using a questionnaire. A trained interviewer (AAK) presented the questionnaire to all participants.

**Clinical Periodontal Parameters**

A calibrated and trained investigator (MA) masked to the study groups performed the periodontal clinical examinations. The overall κ value for intra-examiner...
reliability was 0.91. Full-mouth PI, BOP, PD, and AL were measured at six sites (mesio-buccal, mid-buccal, disto-buccal, disto-lingual/palatal, mid-lingual/palatal, and mesio-lingual/palatal) on all maxillary and mandibular teeth. A graded probe was used to measure PD to the nearest millimeter. Broken teeth with embedded root remnants were excluded.

**Radiographic Parameters**
Full-mouth digital bitewing radiographs were taken and viewed on a calibrated computer screen using a software program.** MBL (defined as the vertical distance from 2 mm below the cemento-enamel junction [CEJ] to the most apical part of marginal bone) was measured on all teeth. Surfaces of teeth on which the CEJ or the bone crest was not visible due to technical reasons (such as dental caries, dental restorations, malocclusion, and/or poor radiographic quality) were excluded. All radiographic assessments were performed by one trained and calibrated investigator (MA). The overall $\kappa$ value for intra-examiner reliability was 0.89.

**HbA1c Levels**
In all groups, HbA1c levels were measured using ion-exchange high-performance liquid chromatography and expressed as percentages.

**Statistical Analyses**
Statistical analysis was performed using a software program.†† Clinical and radiographic periodontal parameters among smokers and never-smokers with and without T2DM were assessed using one-way analysis of variance. Multiple logistic regression analysis evaluated the associations between periodontal inflammation among smokers and never-smokers with and without T2DM (after adjustment for toothbrushing habits [confounder]). For multiple comparisons, Bonferroni post hoc adjustment test was used. Power and sample sizes were calculated.‡‡ With inclusion of 50 patients with T2DM (25 smokers and 25 never-smokers) and 50 controls (25 smokers and 25 never-smokers) (assuming a standard deviation of 1.0%), the study power was estimated to be 85% with a two-sided significance level of 0.05. $P$ values <0.05 were considered statistically significant.

### RESULTS

**General Characteristics of the Study Population**
The mean age, monthly income status, and education levels were comparable among smokers and never-smokers with and without T2DM. The duration of T2DM was 8.5 ± 1.5 years; among smokers and never-smokers, the duration of T2DM was 4.6 ± 1.1 and 10.2 ± 2.5 years, respectively. The duration of smoking habit among patients with T2DM and controls was 12.6 ± 4.8 and 16.4 ± 5.1 years, respectively. Smokers in the control group smoked a significantly greater number of cigarettes (15.5 ± 2.5 cigarettes daily) compared with smokers with T2DM (6.2 ± 2.1 cigarettes daily) ($P$ <0.05). Seventy-eight percent of individuals with T2DM and 88% of controls reported brushing their teeth once daily. None of the participants reported ever having used dental floss (Table 1).

**HbA1c**
Mean HbA1c levels were significantly higher among patients with T2DM (8.2 ± 0.1%) compared with controls (4.4% ± 0.3%) ($P$ <0.05). There was a statistically significant difference in the mean HbA1c levels among smokers with (7.8% ± 0.4%) and without (4.3% ± 0.1%) T2DM ($P$ <0.05) (Table 1). Mean HbA1c levels were significantly higher among patients with T2DM (8.2% ± 0.1%) compared with never-smokers in the control group (4.5% ± 0.1%) ($P$ <0.05). There was no statistically significant difference in mean HbA1c levels among smokers and never-smokers with and without T2DM. Never-smokers with T2DM (8.7% ± 0.2%) had significantly higher mean HbA1c levels than smokers in the control group (4.3% ± 0.1%) ($P$ <0.05). Among never-smokers with and without T2DM, mean HbA1c levels were 8.7% ± 0.2% and 4.5% ± 0.1%, respectively ($P$ <0.05). All patients with T2DM were prescribed conventional allopathic medications for the management of hypoglycemia. Most of the individuals with and without T2DM reported brushing their teeth once a day (Table 1).

**Periodontal Parameters Among Smokers and Never Smokers With and Without T2DM**
Periodontal parameters (PI, BOP, AL, PD ≥4 mm, and MBL) were significantly higher ($P$ <0.01) among patients with T2DM than controls.

Periodontal parameters (PI, BOP, AL, PD ≥4 mm, and MBL) were significantly higher ($P$ <0.01) among smokers with T2DM than smokers and never-smokers in the control group. Never-smokers with T2DM had worse periodontal status ($P$ <0.05) than smokers and never-smokers in the control group (PI, BOP, AL, PD ≥4 mm, and MBL). Among controls, periodontal parameters (PI, AL, PD ≥4 mm, and MBL) were significantly worse ($P$ <0.05) in smokers than never-smokers. In the control group, never-smokers demonstrated significantly more sites with BOP than smokers ($P$ <0.05). These results are summarized in Table 2.
Table 1.

**Sociodemographic Characteristics (mean ± SD, or %) of the Study Participants**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients With T2DM</th>
<th>Controls</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Individuals (n = 50)</td>
<td>Smokers (n = 25)</td>
<td>Never-Smokers (n = 25)</td>
<td>All Individuals (n = 50)</td>
<td>Smokers (n = 25)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
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<tr>
<td>Age (years)</td>
<td>52.6 ± 3.8</td>
<td>50.6 ± 1.8</td>
<td>54.1 ± 3.2</td>
<td>50.5 ± 2.4</td>
<td>48.5 ± 4.8</td>
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<td>Duration of T2DM (years)</td>
<td>8.5 ± 1.5</td>
<td>4.6 ± 1.1</td>
<td>10.2 ± 2.5</td>
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<td>Duration of smoking (years)</td>
<td>12.6 ± 4.8</td>
<td>12.6 ± 4.8</td>
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<td>16.4 ± 5.1</td>
<td>16.4 ± 5.1</td>
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<td>Cigarettes smoked daily (n)</td>
<td>6.2 ± 2.1</td>
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<td>15.5 ± 2.5</td>
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<td>Monthly income (USD)</td>
<td>525 ± 85.4</td>
<td>498.7 ± 90.6</td>
<td>598.5 ± 75.5</td>
<td>585 ± 88.6</td>
<td>530.6 ± 54.7</td>
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<td>Graduate-level education (%)</td>
<td>40</td>
<td>16</td>
<td>24</td>
<td>41</td>
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<td>HbA1c (%)</td>
<td>8.2 ± 0.1†</td>
<td>7.8 ± 0.4*‡</td>
<td>8.7 ± 0.2*‡</td>
<td>4.4 ± 0.3</td>
<td>4.3 ± 0.1</td>
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<td>Treatment of T2DM (%)</td>
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<tr>
<td>Other</td>
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<td>Daily toothbrushing (%)</td>
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<td></td>
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<tr>
<td>Once daily</td>
<td>78</td>
<td>80</td>
<td>76</td>
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<td>Three or more times daily</td>
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<td>Ever used dental floss (%)</td>
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<tr>
<td>Yes</td>
<td>0</td>
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<tr>
<td>No</td>
<td>100</td>
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</table>

* P <0.05 compared with smokers in the control group.
† P <0.05 compared with all individuals in the control group.
‡ P <0.05 compared with never-smokers in the control group.
After stratification for brushing habits, periodontal parameters were comparable among patients with T2DM who brushed their teeth once and twice a day (Figs. 1A and 1B). Among individuals in the control group who brushed their teeth once and twice daily, PI, PD ≥4 mm, and MBL were significantly higher (P < 0.01) among smokers than never-smokers. Never-smokers showed significantly greater numbers of sites with BOP (P < 0.01) than smokers regardless of their daily toothbrushing frequency (Figs. 2A and 2B).

DISCUSSION

The present study is based on the hypothesis that periodontal inflammatory conditions are worse among smokers with T2DM than never-smokers with T2DM. This was mainly speculated because both hyperglycemia and habitual smoking enhance the formation and accumulation of AGEs in the periodontal tissues, which jeopardize periodontal health.9,16 Interestingly, in the present study, clinical and radiologic parameters of periodontal inflammation (PI, BOP, PD ≥4 mm, AL, and

### Table 2.

Clinical Periodontal Status (mean ± SD) Among Smokers and Never-Smokers With and Without T2DM

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients With T2DM</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Individuals (n = 50)</td>
<td>Smokers (n = 25)</td>
</tr>
<tr>
<td>PI (%)</td>
<td>69.4 ± 5.1*</td>
<td>73.4 ± 8.5†‡</td>
</tr>
<tr>
<td>BOP (%)</td>
<td>62.6 ± 4.9*</td>
<td>58.7 ± 4.8‖†‡</td>
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<tr>
<td>Clinical AL (mm)</td>
<td>5.4 ± 1.2*</td>
<td>6.3 ± 0.8‖†‡</td>
</tr>
<tr>
<td>PD ≥4 mm (%)</td>
<td>33.5 ± 5.5*</td>
<td>36.3 ± 4.2‖†‡</td>
</tr>
<tr>
<td>MBL (mm)</td>
<td>6.5 ± 1.2*</td>
<td>7.1 ± 0.5‖†‡</td>
</tr>
</tbody>
</table>

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

Figure 1. A) PI (dark gray bars), BOP (light gray bars), and PD ≥4 mm (striped bars) among smokers and never-smokers with T2DM after stratification for brushing habits. B) Clinical AL (dark gray bars) and MBL (light gray bars) among smokers and never-smokers with T2DM after stratification for brushing habits.
MBL) were comparable among smokers and never-smokers with T2DM. It is pertinent to note that all individuals with T2DM (smokers and never-smokers) included in the present investigation had poorly controlled T2DM (HbA1c ≥6.5%). It is known that persistent hyperglycemia is associated with increased formation and accumulation of AGEs in the periodontal tissues. Therefore, it is likely that AGEs produced and accumulated in the periodontal tissues of smokers and never-smokers with T2DM were comparable. This could be an explanation for the similar periodontal inflammatory parameters among smokers and never-smokers with T2DM.

Among controls, PI, PD ≥4 mm, AL, and MBL were worse in smokers than never-smokers; however, sites with BOP were more often manifested in never-smokers compared with smokers. These results are in accordance with previous studies. A precise mechanism by which habitual smoking increases periodontal inflammation is poorly understood. However, it has been reported that smoking induces endothelial dysfunction, which may initiate an inflammatory response in the vascular walls. Serum levels of immunoglobulin G (particularly immunoglobulin G2, an important antibody against Gram-negative periodontal microbes) have also been reported to be lower in smokers than never-smokers, thereby making them more susceptible to developing periodontal disease. It is noteworthy that a suppressed BOP among smokers (most likely due to the vasoconstrictive effect of nicotine on gingival blood vessels) may make them unaware of the ongoing periodontal breakdown, sometimes until the stage where tooth mobility becomes evident (as a result of profound MBL). It is therefore imperative for health care providers to educate patients about the detrimental effects of smoking on oral health. In addition, routine community-based smoking awareness programs are also warranted for patient/community education purposes.

It is well-known that advancing age, poor education status, and underprivileged SES are significant risk factors for periodontal inflammatory conditions. In this regard, these factors may be considered as confounders when assessing periodontal inflammatory conditions among smokers and never-smokers with and without T2DM. It is emphasized that in the present study, mean age, graduate-level education (more than a 4-year-college degree) status, and SES were comparable in smokers and never-smokers among individuals with and without T2DM. It was therefore perceived that the only parameter that may have influenced the periodontal inflammatory conditions among smokers and never-smokers with and without T2DM was daily toothbrushing frequency. After stratification of data with reference to daily toothbrushing protocols (once and twice daily), it was observed that periodontal parameters (PI, BOP, PD ≥4 mm, AL, and MBL) remained comparable among smokers and never-smokers with T2DM (Figs. 1A and 1B). This outcome also suggests that chronic hyperglycemia seems to be the most likely factor that influenced periodontal inflammation in patients with T2DM, and the role of smoking in this regard was rather secondary. Among controls, there was no significant difference in periodontal parameters in patients who brushed their teeth either once or twice daily (Figs. 2A and 2B).
These results are in accordance with the study by Attin and Hornecker, which reported that toothbrushing once daily is sufficient to maintain oral health and prevent periodontal inflammation.

A limitation of the present study is that all individuals who agreed to participate in the present investigation were males. Although females were also invited to participate in the present study, none of them volunteered. It is known that hormonal changes and the postmenopausal state influence periodontal health status. It is therefore likely that female smokers with T2DM in the postmenopausal phase may exhibit variation in the expression of periodontal disease activity compared with male smokers with T2DM. Furthermore, in the present study, controls were smoking almost twice as many cigarettes (≈15 cigarettes daily) compared with patients with T2DM (≈6 cigarettes daily). It is tempting to hypothesize that smokers with T2DM who smoke ≈15 cigarettes a day may exhibit more intense periodontal inflammation compared with never-smokers with T2DM. However, further randomized controlled trials are warranted to assess a dose-dependent relationship between smoking, periodontal disease, and T2DM.

CONCLUSIONS

Periodontal inflammatory conditions are comparable among smokers and never-smokers with T2DM. Among controls, periodontal inflammation is worse among smokers than never-smokers.

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Correspondence: Dr. Fawad Javed, Division of General Dentistry, Eastman Institute for Oral Health, University of Rochester, Rochester, NY 14642. E-mail: fawad_javed@urmc.rochester.edu.

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