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# Comparison of periodontal and peri-implant inflammatory parameters among patients with prediabetes, type 2 diabetes mellitus and non-diabetic controls

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#### ABSTRACT

**Objective:** The aim was to compare periodontal and periimplant inflammatory parameters (plaque index [PI], bleeding on probing [BOP], probing depth [PD] and marginal bone loss [MBL]) among patients with prediabetes, type-2 diabetes mellitus (T2DM) and non-diabetic controls.

**Materials and methods:** Forty-five patients with prediabetes (Group-1), 43 patients with T2DM (Group-2) and 42 controls (Group-3) were included. Demographic data was recorded using a questionnaire. Full mouth and periimplant clinical (PI, BOP and PD) were assessed and the radiographic MBL were measured on digital radiographs. In all groups, haemoglobin A1c (HbA1c) levels were also measured. *p* values less than .05 were considered statistically significant.

**Results:** The mean HbA1c levels of participants in groups 1, 2 and 3 were 6.1%, 8.4% and 4.8%, respectively. The mean duration of prediabetes and T2DM among patients in groups 1 and 2 were  $1.9\pm0.3$  and  $3.1\pm0.5$  years, respectively. Periodontal and periimplant PI, BOP, PD and MBL were higher in groups 1 (p < .05) and 2 (p < .05) than group 3. There was no difference in these parameters in groups 1 and 2.

**Conclusions:** Periodontal and periimplant inflammatory parameters were worse among patients with prediabetes and T2DM compared with controls; however, these parameters were comparable among patients with prediabetes and T2DM.

# Introduction

Studies have shown that dental implants therapy is no longer restricted for systemically healthy individuals [1,2]; and patients with systemic disorders such as diabetes mellitus and prediabetes are also potential candidates for oral rehabilitation with dental implants [1,3,4]. Results from a recent 24-month follow-up study showed that dental implants can remain clinically and radiographically stable in patients with type-2 diabetes mellitus (T2DM) in a manner similar to non-diabetic individuals (controls) [2]. Similarly, results from another 1-year follow-up study showed that success rates of dental implants placed among patients with and without prediabetes are comparable [1]; however, it is noteworthy that in these studies [1,2], hyperglycaemic patients (patients with prediabetes and T2DM) were compared with normoglycaemic individuals (non-diabetic controls). Results from experimental studies [5,6] have shown that the interaction between advanced glycation endproducts (AGEs) (produced as a result of persistent hyperglycaemia) and their receptors are significantly higher in the inflamed periodontal tissues of rats with induced hyperglycaemia compared with rats with normal glycaemic levels. It is therefore hypothesized that the severity of peri-implant clinical (plaque index [PI], bleeding on probing [BOP], probing

depth [PD]) and radiographic (marginal bone loss [MBL]) parameters vary among patients with prediabetes (haemoglobin A1c [HbAc] levels 5.7% and 6.4%) and those with T2DM (HbA1c levels  $\geq$ 6.5%) [7].

In a recent in vitro study, Chiu et al. [8], investigated the effect of hyperglycaemia and AGEs on the amounts of interleukin (IL)-6 produced in human gingival fibroblasts (HGFs). The results showed that hyperglycaemia significantly increased the production of IL-6 by HGFs compared with HGFs under normoglycaemic conditions. Moreover, in the study by Promsudthi et al. [9], hyperglycaemia increased the expression of toll-like receptors (TLRs) in periodontal tissues, which contribute to a greater inflammatory response in patients with hyperglycaemia as well as periodontal disease. In the present study, it is hypothesized that (a) peri-implant PI, BOP, PD and MBL are worse among patients with prediabetes and T2DM compared with controls; (b) peri-implant PI, BOP, PD and MBL are worse among patients with poorly controlled T2DM compared with patients with prediabetes since HbA1c levels are higher in the former group of individuals.

With this background, the aim of the present cross-sectional cohort study was to compare peri-implant inflammatory parameters among patients with prediabetes, T2DM and non-diabetic controls.

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# ARTICLE HISTORY

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#### **KEYWORDS**

Alveolar bone loss; diabetes mellitus type 2; gingival bleeding on probing; prediabetic state; periodontal disease

# **Materials and methods**

# **Ethical guidelines**

The study was approved by the Research Ethics Review Committee of the College of Dentistry, King Saud University, Riyadh Saudi Arabia. An information sheet printed in simple English and Arabic that described the purpose and the methods used in the present study was provided to individuals visiting the College of Dentistry, King Saud University, Riyadh, Saudi Arabia. The information sheet also clearly stated that participation is completely voluntary and the individuals reserved the right to withdraw their participation at any stage of the investigation without any consequence/s. The above information was also verbally conveyed to all individuals following which a consent form was presented to volunteering individuals. It was mandatory for all individuals to have read the information sheet and sign the consent form prior to their inclusion in the present investigation.

## Inclusion and exclusion criteria

The inclusion criteria were as follows (a) patients having undergone dental implant therapy; (b) individuals with medically diagnosed prediabetes (HbA1c levels between 5.7% and 6.4%; (c) individuals with medically diagnosed T2DM (HbA1c levels  $\geq$ 6.5%) [7]; (d) nondiabetic controls (HbA1c levels 4% to 5%) [7]. Exclusion criteria were (a) patients with self-reported systemic diseases such as acquired immune deficiency syndrome, cardiovascular disorders, epilepsy, hepatic disorders, renal disorders and obese/overweight individuals; (b) use of antibiotics and/or steroids within the past 90 days; (c) patients have undergone periodontal therapy within the past 90 days; (d) patients with crowding of teeth or occlusal trauma; (e) edentulous individuals; (f) habitual tobacco smoking and/or smokeless tobacco use; (g) habitual alcohol consumption; (h) pregnancy and/or lactation and (i) maxillary and mandibular third molars.

# Study participants and groups

A convenience sample case-control study involving patients with prediabetes (Group-1), T2DM (Group-2) and controls (Group-3) was performed at the College of Dentistry, King Saud University, Riyadh, Saudi Arabia. The study participants were recruited from a local residential area in Riyadh, Saudi Arabia. Clinical and radiographic examinations were performed at the College of Dentistry, King Saud University, Riyadh, Saudi Arabia. All participants who reported to have prediabetes or T2DM were requested to present their medical records for verification.

# Questionnaire

Data regarding age, gender, education status (graduate level education— post-4 year college degree), duration of prediabetes or T2DM, family history of prediabetes or T2DM, treatment of prediabetes or T2DM recommended by healthcare provider/s and daily frequency of tooth brushing and flossing were collected using a questionnaire. A trained interviewer (TA) presented the questionnaire to all participants.

### **Clinical periodontal parameters**

A trained and calibrated examiner (TA) who was blinded to the study groups performed the periodontal and peri-implant clinical examinations. The overall *kappa* value for intraexaminer reliability was 0.9. Full-mouth and peri-implant PI [10], BOP [11] and PD [12] were measured at six sites (mesiobuccal, mid-buccal, distobuccal, distolingual/palatal, mid-lingual/ palatal and mesiolingual/palatal) per tooth/implant. PD was measured to the nearest millimeter using a graded probe (Hu-Friedy, Chicago, IL) [13]. Number of missing teeth (MT) was also counted in all groups. Broken down teeth with embedded roots remnants were considered missing.

# Marginal bone loss

Digital bitewing radiographs (Ektaspeed plus; Kodak, Rochester, NY) were taken and viewed on a calibrated computer screen (Samsung SyncMaster digital TV monitor, Suwon City, Gyeonggi-do, Korea) using a software program (Image Tool 3.0, Department of Dental Diagnostic Science, University of Texas Health Science, Center, San Antonio, TX). MBL (defined as the vertical distance from 2 mm below the cementoenamel junction (CEJ) to the most crestal part of marginal bone [13] was measured on all teeth at baseline and . On implant surfaces mesial and distal MBL was measured as the vertical distance from 2 mm below the implant abutment junction to the most crestal part of marginal bone [14]. Teeth on which the CEJ and/or the bone crest were not visible due to technical reasons (such as dental caries, dental restorations, malocclusion and/or poor radiography guality) were excluded. All radiographic were assessed by a trained and calibrated investigator (FV). The overall kappa score for intraexaminer reliability was 0.92.

# Haemoglobin A1c levels

In all groups, HbA1c levels were measured using an HbA1c analyzer kit (Quo-Test, EKF Diagnostics, Magdeburg, Germany) by a trained investigator (TA). The overall *kappa* score for intraexaminer reliability was 0.95.

#### Statistical analysis

Statistical analysis was performed using a software program (SPSS v.18, IBM, Chicago, IL). Clinical and radiographic periodontal parameters among patients in groups 1, 2 and 3 were assessed using Kruskall–Wallis test. Multiple logistic regression analysis was also performed to investigate the associations between periodontal/peri-implant inflammation among patients in groups 1, 2 and 3 after adjustment of the data for tooth brushing habits. For multiple comparisons, Bonferroni's *post hoc* adjustment test was performed. Power and sample sizes were calculated using a computer software (nQuery Advisor 6.0, Statistical Solutions, Saugas, MA).

With inclusion of 40 individuals per group (assuming a standard deviation of 1.0%), the study power was estimated to be 90% with a two-sided significance level of .05. p values < .05 were considered statistically significant.

# Results

# General characteristics of the study cohort

In total, 45 patients in Group 1, 43 in Group 2 and 42 in Group 3 were included. The mean age and HbA1c levels of participants in groups 1, 2 and 3 were  $53.4 \pm 3.5$ ,  $51.1 \pm 1.6$ and  $50.6 \pm 2$  years and 6.1%, 8.4% and 4.8%, respectively. The mean duration of prediabetes and T2DM among patients in groups 1 and 2 were  $1.9 \pm 0.3$  and  $3.1 \pm 0.5$  years, respectively. A family history of diabetes was reported by 28 individuals in group 1, 31 individuals in group 2 and 7 individuals in group 3. Three, 5 and 26 individuals in groups 1, 2 and 3, respectively reported to have attained graduate level education (Table 1). All individuals in group-1 (n = 45) were advised by their healthcare physicians to maintain blood glucose levels via dietary controls. In group 2, all participants were prescribed anti-hyperglycaemic medications for the treatment of T2DM and were also advised to observe dietary control. Tooth brushing once daily was reported by 86.7%, 81.4% and 80.9% individuals in groups 1, 2 and 3, respectively. None of the participants in groups 1, 2 and 3 reported to floss their teeth.

#### Implant-related characteristics

All implants were platform-switched and were loaded approximately 3 months after placement. All implants had moderately rough surfaces and their lengths and diameters ranged between 10–14 mm and 3.3–4.1 mm, respectively. All implants were placed at the level of the alveolar crest. All participants had implants placed in the areas of missing mandibular premolars or molars. In groups 1, 2 and 3 a total of 45 (39 implants replacing missing first molars and 6 replacing

Table 1. General characteristics of the study population.

the first premolar), 43 (28 implants replacing missing first molar, 5 implants replacing the missing second molars and 10 replacing the first premolar) and 42 implants (30 implants replacing missing first molars and 6 replacing the first premolar) were placed. In groups 1, 2 and 3, the implants had been in function since  $6.2\pm0.3$  years,  $7.1\pm0.4$  years and  $6.5\pm0.2$  years, respectively.

# Periodontal inflammatory parameters among participants in groups 1, 2 and 3

Scores of full-mouth PI, BOP, PD, MBL and number of MT were statistically significantly higher among patients in groups 1 (p < .05) and 2 (p < .05) compared with group 3. There was no statistically significant difference in scores of PI, BOP, PD, MBL and number of MT a full mong participants in groups 1 and 2 (Table 2).

# Logistic regression model of periodontal inflammatory parameters among participants in groups 1, 2 and 3 after adjustment for daily frequency of tooth brushing

Among individuals who reported to brush their teeth once and twice daily, PI, BOP, PD, MBL and numbers of MT were statistically significantly higher among individuals in groups 1 (p < .05) and 2 (p < .05) compared with group-3. There was no statistically significant difference in PI, BOP, PD, MBL and numbers of MT among individuals who reported to brush their teeth once compared with those who brushed twice daily in groups 1 and 2 (Table 3).

# Peri-implant inflammatory parameters among participants in groups 1, 2 and 3

Scores of peri-implant PI, BOP, PD and MBL were statistically significantly higher among patients in groups 1 (p < .05) and 2 (p < .05) compared with group-3. There was no statistically significant difference in scores of peri-implant PI, BOP, PD and MBL among participants in groups 1 and 2 (Table 4).

Parameters	Group-1 (patients with prediabetes)	Group-2 (patients with T2DM)	Group-3 (non-diabetic controls)	
Number of participants	45	43	42	
Mean age (±SD) in years	$53.4 \pm 3.5$	50.6 ± 2	51.1 ± 1.6	
Mean duration $(\pm SD)$ of the endocrine disorder in years	$1.9 \pm 0.3$	$3.1 \pm 0.5$	_	
Mean haemoglobin A1c levels (±SD)	$6.1 \pm 0.2$	8.4 ± 1.3	$4.5 \pm 0.1$	
Family history of diabetes (n)	28	31	7	
Graduate level education (n)	3	5	26	

SD: standard deviation.

#### Table 2. Scores of periodontal inflammatory parameters among participants in groups 1, 2 and 3.

Parameters	Group 1 (patients with prediabetes)	Group 2 (patients with T2DM)	Group 3 (non-diabetic controls)	
Number of participants	45	43	42	
Plaque index in percentage (Mean $\pm$ SD)	$46.5 \pm 6.4^{*}$	$49.2 \pm 4.5^{*}$	$20.4 \pm 1.7$	
Bleeding on probing in percentage (Mean $\pm$ SD)	$50.6 \pm 2.7^{*}$	$55.3 \pm 3.4^{*}$	$23.5 \pm 0.8$	
Probing depth in mm (Mean $\pm$ SD)	$5.2 \pm 0.8^{*}$	$5.8 \pm 1.4^{*}$	$2.5 \pm 0.5$	
Marginal bone loss in mm (Mean $\pm$ SD)	$4.2 \pm 0.7^{*}$	$4.7 \pm 0.3^{*}$	$2.2 \pm 0.2$	
Number of missing teeth (Mean $\pm$ SD)	$10.4 \pm 0.8^{*}$	$13.2 \pm 1.4^{*}$	4.8 ± 1.2	

\*Compared with Group 3 (p < .05).

SD: standard deviation; mm: millimeters.

Table 3. Logistic regression model of	periodontal inflammatory	parameters among	participants in groups	1, 2 and 3 adjusted b	v tooth brushing habits.

	Tooth brushing once daily			Tooth brushing twice daily			
Periodontal parameters (Mean ± SD)	Group-1 (patients with prediabetes)	Group-2 (patients with T2DM)	Group-3 (non-diabetic controls)	Group-1 (patients with prediabetes)	Group-2 (patients with T2DM)	Group-3 (non-diabetic controls)	
Number of participants	39	35	34	6	8	8	
Plague index in percentage	$45.2 \pm 4.6^{a}$	$51.3 \pm 1.4^{a}$	$22.3 \pm 1.2$	$42.6 \pm 5.1^{b}$	$47.6 \pm 3.4^{b}$	$18.5 \pm 1.1$	
Bleeding on probing in percentage	$54.3 \pm 3.2^{a}$	$61.6 \pm 2.1^{a}$	$26.2 \pm 0.8$	$47.2 \pm 2.8^{b}$	$54.4 \pm 3^{b}$	$24.5 \pm 0.6$	
Probing depth in mm	$5.6 \pm 0.5^{a}$	$6.2 \pm 0.5^{a}$	$2.2 \pm 0.2$	$4.6 \pm 0.6^{b}$	$5.1 \pm 0.5^{b}$	$1.8 \pm 0.3$	
Marginal bone loss in mm	$4.6 \pm 0.6^{a}$	$4.4 \pm 0.3^{a}$	$2.4 \pm 0.3$	$4.2 \pm 0.4^{b}$	$3.8 \pm 0.4^{b}$	$1.6 \pm 0.3$	
Number of missing teeth	$12.4 \pm 1.6^{a}$	$13.5 \pm 0.8^{a}$	$5.8\pm0.2$	$9.6 \pm 0.6^{b}$	$9.4\pm0.4^{b}$	$2.1 \pm 0.2$	

<sup>a</sup>Compared to controls who reported to brush their teeth once daily.

<sup>b</sup>Compared to controls who reported to brush their teeth twice daily.

SD: standard deviation; mm: millimeters.

Table 4. Scores of peri-implant inflammatory parameters among participants in groups 1, 2 and 3.

Peri-implant parameters	Group-1 (patients with prediabetes)	Group-2 (patients with T2DM)	Group-3 (non-diabetic controls)
Number of participants (n)	45	43	42
Plaque index (mean $\pm$ SD) in percentage	$35.5 \pm 4.5^{*}$	$33.4 \pm 2.8^{*}$	19.2 ± 1.5
Bleeding on probing (mean $\pm$ SD) in percentage	$36.4 \pm 4.1^{*}$	$33.3 \pm 3.5^{*}$	$15.2 \pm 0.8$
Probing depth (mean $\pm$ SD) in mm	$4 \pm 0.4^{*}$	$4.2 \pm 0.2^{*}$	$2.1 \pm 0.1$
Marginal bone loss (mean $\pm$ SD) in mm	$3.4 \pm 0.6^{*}$	$3.5 \pm 0.4^{*}$	1.6 ± 0.2

\*Compared with Group-3 (p < .05).

SD: standard deviation; mm: millimeters.

Table F Logistic regression model of	f nori implant inflammatory narameters	among participants in groups 1 2 and	2 adjusted by teath brushing habits
Table 5. Logistic regression model of	f peri-implant inflammatory parameters	among participants in groups 1, 2 and	3 adjusted by tooth brushing habits.

	Tooth brushing once daily			Tooth brushing twice daily		
Parameters	Group-1 (patients with prediabetes)	Group-2 (patients with T2DM)	Group-3 (non-diabetic controls)	Group-1 (patients with prediabetes)	Group-2 (patients with T2DM)	Group-3 (non-diabetic controls)
Number of participants	39	35	34	6	8	8
Plaque index (mean $\pm$ SD) in percentage	$43.6 \pm 4.2^{a}$	$48.5 \pm 3.7^{a}$	$16.2 \pm 1.5$	$40.6 \pm 4.2^{b}$	41.5 ± 4 <sup>b</sup>	$14.2 \pm 0.9$
Bleeding on probing (mean $\pm$ SD) in percentage (range)	$50.5 \pm 3.6^{a}$	$57.2 \pm 2.8^{a}$	$20.2 \pm 1.2$	51.1 ± 4.8 <sup>b</sup>	49.8 ± 2.3 <sup>b</sup>	$18.4 \pm 1.1$
Probing depth (mean $\pm$ SD) in mm	$4.5 \pm 0.6^{a}$	$4.7 \pm 0.5^{a}$	$1.6 \pm 0.1$	$4.2 \pm 0.2^{b}$	$4.6 \pm 0.4^{b}$	$1.9 \pm 0.2$
Marginal bone loss (mean $\pm$ SD) in mm	$4.6 \pm 0.5^{a}$	$4.4\pm0.4^{\rm a}$	$2.4 \pm 0.6$	$4.2 \pm 0.8^{b}$	$3.8 \pm 0.6^{b}$	$1.6 \pm 0.2$

<sup>a</sup>Compared to controls who reported to brush their teeth once daily.

<sup>b</sup>Compared to controls who reported to brush their teeth twice daily.

SD: standard deviation; mm: millimeters.

# Logistic regression model of peri-implant inflammatory parameters among participants in groups 1, 2 and 3 after adjustment for daily frequency of tooth brushing

There was no statistically significant difference in peri-implant PI, BOP, PD and MBL among individuals who reported to brush their teeth once compared with those who brushed twice daily in groups 1 and 2 (Table 5). In group-3, scores of peri-implant PI, BOP, PD and MBL were statistically significantly higher among individuals who reported to brush their teeth once compared with those who brushed twice daily.

The peri-implant inflammatory parameters were comparable with their respective periodontal parameters among individuals in groups 1, 2 and 3 (Tables 2 and 4).

# Discussion

The present study was based on the hypothesis that (a) periimplant PI, BOP, PD and MBL are worse among patients with prediabetes and T2DM compared with controls; (b) periimplant PI, BOP, PD and MBL are worse among patients with poorly controlled T2DM compared with patients having

prediabetes since HbA1c levels are higher in the former group of individuals. The present results support the first hypothesis and several studies [13,15-18] have shown that chronic hyperglycaemia (as observed among patients with prediabetes and poorly controlled T2DM) is a risk-factor for periodontal and per-implant tissue inflammation. One explanation in this regard is that chronic hyperglycaemia increases the production of proinflammatory cytokines such as IL-6 by human gingival fibroblasts as compared to normal glucose [8]. Moreover, results from experimental studies [5,6] have reported that the interaction between AGEs and their receptors are significantly higher in the inflamed periodontal tissues of rats with induced hyperglycaemia compared with rats with normal glycaemic levels. The same mechanisms have been associated with peri-implant inflammation thereby jeopardizing implant stability [19,20]. Furthermore, Promsudthi et al. [9] reported that hyperglycaemia increases the expression of TLRs (which contribute to a greater inflammatory response in patients with hyperglycemia as well as periodontal disease) in periodontal tissues. This suggests that as the severity of hyperglycaemia increases, the periodontal and peri-implant inflammatory response is also expected to

rise. We therefore speculated that periodontal and periimplant inflammatory parameters are worse in patients with T2DM compared with prediabetic individuals (second hypothesis). However, the present result showed that periodontal and peri-implant scores of PI, BOP, PD and MBL were comparable among patients in groups 1 and 2. Various explanations can be posed in this regard. It has been reported that there is a statistically significant relationship between duration of hyperglycaemia and the severity of periodontal inflammation [21,22]. According to Al-Shammari et al. [21], periodontal inflammatory parameters (MT and clinical attachment loss) are significantly higher among patients with a longer duration of T2DM ( $\geq$ 5 years) compared with individuals with a shorter duration of diabetes (<5 years). It is noteworthy that in the present study, the duration of prediabetes and T2DM among patients in group 1 and group 2 was approximately 2 years and 3 years, respectively. It is therefore hypothesized that patients in group 2 would have would have demonstrated significantly worse periodontal and periimplant inflammation than individuals in group 1, if the duration of T2DM was at least 5 years. Further studies are warranted to test this hypothesis. It is noteworthy that PI was significantly higher among patients with prediabetes and T2DM compared with controls. It is well-known that dental plaque harbous microbes (such as Porphyromonas gingivlis and Prevotella intermedia) that have been associated with the aetiology of periodontal and periimplant diseases [23-25]. Therefore, the inflammatory conditions reported in the present study groups may well depend on the oral biofilm deposits and not merely on the glycaemic status. Hence, further studies are warranted in this regard.

It is well-known that poor education status and family history of diabetes are significant risk factor of prediabetes, T2DM and periodontal disease.[13,26-28] The present study supports these results since a family history of diabetes was reported by approximately 62% and 72% patients in groups 1 and 2, respectively compared with individuals in group 3  $(\sim 17\%)$ . Moreover, graduate level education was more often reported by controls (~62%) compared with patients in groups 1 and 2 ( $\sim$ 7% and  $\sim$ 9%, respectively). It is therefore essential to educate patients (particularly those with a family history of diabetes) about the possible risk factors of prediabetes and diabetes and their influence on overall health. Routine community-based health awareness programs can play a role in this regard. An interesting finding in the present study was that even after stratifying the data with reference to tooth brushing habits, periodontal and peri-implant inflammatory parameters remained comparable among patients in groups 1 and 2 compared with controls. One explanation is that there were only a limited number of patients in groups 1 ( $\sim$ 13%) and 2 ( $\sim$ 19%) who reported to brush their teeth twice daily. Moreover, since the education status was poorer among patients in groups 1 and 2 compared with the controls, it is possible that their perception of oral hygiene maintenance also varied compared with controls.

A limitation of the present study was that strict eligibility criteria were imposed for patient selection. It is well-known that habits such as tobacco smoking and smokeless tobacco consumption are risk factors for periodontal disease [29,30]. Moreover, since most of the participants in the present study were male, it is exigent to assess whether or not there is a difference in the severity of periodontal disease among males and females with prediabetes and T2DM. Further studies are warranted in this regard. It is recommended that patients with chronic hyperglycaemia (such as those with prediabetes and T2DM) should be educated about the detrimental effects of chronic hyperglycaemia on health; and should be encouraged to maintain glycaemic levels within the normal range (HbA1c levels 4% to 5%). Routine visits to oral healthcare providers and physicians may also beneficial in this regard.

In conclusion, periodontal and periimplant inflammatory parameters were worse among patients with prediabetes and T2DM compared with controls; however, these parameters were comparable among patients with prediabetes and T2DM.

#### **Disclosure statement**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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