Stability and bone loss around submerged and non-submerged implants in diabetic and non-diabetic patients: a 7-year follow-up

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Abstract: To evaluate peri-implant bone loss (PIBL) and stability around submerged and non-submerged dental implants in patients with and without type 2 diabetes mellitus (T2DM). Thirty-five T2DM and non-diabetic (NT2DM) patients were included in this study. Demographic data were recorded using a questionnaire and PIBL was measured on digital radiographs. Resonance frequency analysis (RFA) was carried out for each implant at the time of fixture placement and at 3 months in both groups. P values less than 0.05 were considered statistically significant. One hundred and eighteen dental implants with a mean height of 10 to 12 mm and 3.3 to 4.1 mm in diameter were placed. The comparison of the mean RFA values at baseline and at 3 months was statistically significant (p = 0.008) in T2DM patients. The inter-group mean RFA values at baseline and at 3 months were not significant (p > 0.05). PIBL was significantly high in T2DM as compared to NT2DM patients at each follow-up (p < 0.05). At 2, 3, and 7 years, non-submerged dental implants showed significantly high PIBL in T2DM patients as compared to NT2DM individuals (p<0.05). The results of the present clinical study demonstrate increased PIBL around non-submerged single-tooth implant-supported restorations in T2DM patients, which may be due to the immune inflammatory status.

Keywords: Dental Implants; Diabetes Mellitus, Type 2; Resonance Frequency Analysis.

Introduction

Type 2 diabetes mellitus (T2DM) has been on the rise and has become a major public health problem. New estimates of T2DM among adults show a high disease burden, especially in developing countries.[1] Recent data published by the World Health Organization (WHO) reveal an estimated 7 million adults have diabetes mellitus and more than 3 million Saudi Arabians are prediabetic. This is an alarming number as Saudi Arabia is ranked second in the Middle East and has the seventh highest rate of T2DM in the world.[2] Patients with T2DM are associated with an increased risk of periodontal disease and tooth loss.[3]

Type 2 diabetes mellitus demands special attention in dental treatment, particularly when dental implants are to be placed. Interestingly, studies have

reported that dental implant therapy is not restricted to systemically healthy individuals; T2DM patients are also potential candidates for dental implant therapy.[4,5] However, the underlying pathophysiology that increases the risk of peri-implant tissue loss in subjects with T2DM cannot be disregarded. Research indicates that T2DM has been associated with the formation and accumulation of advanced glycation end products (AGEs), which contribute to its pathogenesis and to abnormal periodontal wound healing.[6,7] These end products reduce the production of matrix proteins such as collagen and osteocalcin by gingival and periodontal fibroblasts.[8] It has also been suggested that T2DM patients present with persistent inflammatory response, significant attachment loss, and increased alveolar bone resorption.[9]

There appears to be limited and controversial data available in the literature regarding peri-implant outcomes in patients with T2DM. Dental implant therapy was evaluated in T2DM patients in a 4-month prospective cohort study and revealed high clinical success.[10] Similarly, results from a recent 24-month study showed that dental implants can remain clinically and radiographically stable in T2DM patients in a manner that is similar to that observed in non-diabetic (NT2DM) individuals.[11,12] However, these studies were conducted for a short follow-up period and, therefore, studies with a longer follow-up period may help to elucidate peri-implant outcomes and stability of dental implants in T2DM as compared to NT2DM patients. Thus, the aim of the present 7-year prospective observational study was to evaluate peri-implant bone loss (PIBL) and stability around submerged and non-submerged dental implants in T2DM and NT2DM patients.

Methodology

Trial design and study setting

The present study was performed in accordance with the Declaration of Helsinki revised in 2013 for experimentation involving human subjects. This was a 7-year prospective observational study which was designed, conducted, and reported following the 'Strengthening the Reporting of Observational Studies in Epidemiology' (STROBE) checklist.[13] The clinical trial was conducted in King Abdulaziz Medical City, Dental Center, Riyadh, Saudi Arabia.

The study protocol was initially reviewed and later approved by the ethics committee of King Abdullah International Medical Research Center, Saudi Arabia.

Inclusion and exclusion criteria

Adult patients were recruited using the following criteria: a) diagnosis of T2DM (test group) and NT2DM (control group) according to the American Diabetes Association;[14] b) HbA1c levels > 6.0% for T2DM patients and ≤ 6.0% for NT2DM patients at the time of surgery;[10] c) single-tooth implant-supported restoration; c) adequate bone dimensions for implant placement without bone grafting; and e) implant sites with ≥ 3 months of healing. Patients with any medical condition other than T2DM, such as acquired immune deficiency syndrome/HIV, cardiovascular disorders, and renal diseases, were excluded. In addition, patients with periodontal disease, former or current smoking status, and who had used medications such as steroids, non-steroidal anti-inflammatory drugs, and antibiotics within the past 6 months were also excluded.

Study participants

Subjects were recruited from the National Guard community, Riyadh, Saudi Arabia from June 2009 to January 2011. Eligible participants were informed about the purpose and process of the study in the local language (Arabic) or in English, both verbally and in writing. A written informed consent was obtained. The study subjects signed a consent form and were allowed to withdraw from the research project at any time without any consequences.

Questionnaire

A trained interviewer collected information on gender, age, duration of diabetes, type of diabetes medication, previous complications from diabetes, and daily oral hygiene status of all study participants. Medical and dental histories were also recorded in a questionnaire sheet.

Measurement of hemoglobin A1c levels

HbA1c levels were measured in both T2DM and NT2DM patients using ion-exchange high-performance liquid chromatography (Adams A1c HA8160, Diabetes Mode, Arkray, Inc., Kyoto, Japan) and were expressed as percentages.

Surgical procedure

A total of 118 dental implants (ITI ® Straumann Dental Implant System, Wandenburg, Switzerland) were placed in 70 patients (35 T2DM and 35 NT2DM patients) at the dental implant clinic between 2009 and 2011. All implants were placed according to the manufacturer's instructions. A traditional two-stage surgical protocol was used for submerged implant placement, whereas a one-stage surgical protocol was used for non-submerged implant placement. All surgical procedures were performed under local anesthesia. A crestal incision was made followed by elevation of a full-thickness mucoperiosteal flap. After the implant sites were prepared, all implants were placed using a torque controller. The mucosa was sutured after the implant placement. Some implants were placed with a submerged protocol and topped with a closure screw to avoid loading during the healing process, while some were placed with a non-submerged protocol, where the cover screw around the soft tissue was left exposed. The implants were left to heal for 3 months in the mandible and for 6 months in the maxilla until osseointegration was complete. Healing abutments were placed in the second stage. Final impressions were made, and the crowns were fabricated using traditional laboratory methods. After implant placement, radiographs were taken at the moment of prosthetic placement following standardized parameters to compare crestal bone levels at 1-year and 7-year follow up.

Postoperative care

After implant placement and suturing, each patient received 625 mg of Augmentin and 400 mg of Ibuprofen to be taken three times daily for 7 days, and a 0.2% chlorhexidine (Deef®, AlQassim, Saudi Arabia) mouthwash was prescribed to all patients for 2 weeks. Patients were also asked to brush their teeth gently with antiseptic toothpaste. Sutures were removed 8–10 days after surgery. The patients were recalled at 1, 2, 3, and 7 years after implant placements. The criteria for successful implant placement were stable implants and superstructures with no symptoms of pain and without any signs of inflammation and purulent discharge, loss of no more than 1 mm bone around the implant in the first year, and no radiolucency around implants.

Resonance frequency measurements

Resonance frequency measurements were made for each implant at the time of fixture placement and at 3 months in both groups. The instrumentation used to perform the measurements had been previously described by Meredith et al.[15] Measurements were carried out by screwing a transducer to the top of the abutment. The transducer beam comprised a small L-shaped cantilever to which two piezoceramic elements had been attached. One of the elements was excited by a sinewave signal of amplitude 1.0 v, whose frequency ranged from 6 to 12 kHz in steps of 25 Hz. The response of the beam was measured by the second piezoceramic element and the resonance frequency of the transducer/implant system was calculated from the peak amplitude of the signal.

Peri-implant bone loss

Peri-implant bone loss was defined as the distance from the widest supracrestal part of the implant to the alveolar crest.[16] Digital intraoral radiographs were taken using the long-cone paralleling technique. To prepare parallel radiographs, a film holder (Dentsply Rinn, PA, USA) was used to standardize the angulation between the X-ray beam and the film. The central X-ray beam was directed perpendicularly to the film and long axis of the implant. At the implant sites, both mesial and distal PIBL were analyzed at 20x magnification using a computer software program (CorelDraw 11.0, Corel Corp and Coral Ltd, Ottawa, Canada).

Statistical analysis

Statistical analyses were carried out using the SPSS for Windows, v.20.0 (IBM, Chicago, IL, USA). Data were expressed as means and standard deviations. Normality of distribution of the variables was tested with Shapiro-Wilk tests and confirmed with Q-Q plots. For the purpose of analysis, the patients were split into subgroups according to diabetic status and position of fixture (submerged/non-submerged). PIBL was analyzed to identify any associations with T2DM and position of fixture and the time following implant placement (1, 2, 3, and 7 years). Between-group comparison of means was verified with the Mann-Whitney U test. The level of significance was set at 0.05.

Results

Out of 101 patients, 70 signed the informed consent form and participated in the study. The study groups consisted of 35 patients with T2DM (22 males and 13 females) and 35 NT2DM patients (24 males and 11 females) who were treated with dental implants (Figure). The mean age of T2DM and NT2DM patients was 54.6 years and 46.8 years, respectively. With regards to gender distribution, both groups showed a higher prevalence of men than of women. The mean duration of diabetes in T2DM patients was 12.6 years. Twice-daily toothbrushing was reported by 71% and 42% of NT2DM and T2DM patients, respectively (Table 1). None of the patients experienced allergy to penicillin medication.

A total of 118 dental implants with a mean height of 10 to 12 mm and 3.3 to 4.1 mm in diameter were placed. Sixty single-tooth implants were restored in the mandible 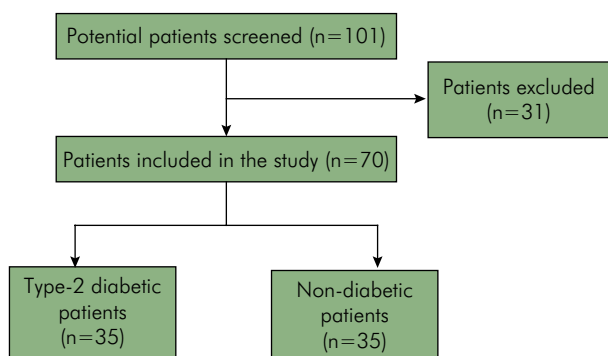while 58 single-tooth implants were placed in the maxilla (Table 2). Of the 118 implants evaluated, 117 (99.15%) survived for 7 years. One implant failure occurred at 6 months following implant placement in the T2DM group. This implant was successfully replaced and restored without further complications, and was evaluated at 1, 2, 3, and 7 years.

The comparison of the mean RFA values at baseline and at 3 months in T2DM patients was statistically significant (p = 0.008). The between-group mean RFA values at baseline and at 3 months was not significant (p > 0.05) (Table 2).

Results for PIBL are shown in Table 3. PIBL was found to increase in both groups. However, there was a statistically significant difference between both groups in all follow-up periods. PIBL varied from 0.53 mm after the first year (p = 0.004) to 1.1 mm after 7 years (p = 0.000) in T2DM patients (Table 3).

Table 4 shows PIBL between submerged and non-submerged dental implants at 1, 2, 3, and 7 years in T2DM and NT2DM patients. After the first year of assessment, there was a statistically significant difference for both submerged (p = 0.026) and non-submerged (p = 0.014) dental implants between T2DM and NT2DM groups. At 2, 3, and 7 years, only non-submerged dental implants showed significantly high PIBL in T2DM patients as compared to NT2DM individuals (p < 0.05) (Table 4).

Discussion

The aim of the present 7-year observational study was to evaluate PIBL and stability around submerged and non-submerged dental implants in T2DM and NT2DM patients. To our knowledge, this is the first study to evaluate PIBL and stability around submerged and non-submerged dental implants placed in T2DM and NT2DM patients. The findings of the present study showed that PIBL was significantly greater in T2DM as compared to NT2DM patients. Moreover, at 7 years, non-submerged dental implants showed more bone loss in T2DM than in NT2DM patients.

Replacing missing teeth with dental implants has been shown to be safe and effective, with a high success rate, despite certain factors that can influence the outcomes, including certain effects of T2DM on the osseointegration process in diabetic patients

Figure. Study flow diagram showing recruitment details.

Table 1. Demographic characteristics of study participants.

Characteristics	Non-diabetic	Type 2 diabetes
Number of patients	35	35
Gender (M/F)	24/11	22/13
Mean age (years)	46.8±8.1	54.6±9.9
HbA1c levels (%)	4.7	8.2
Duration of diabetes (years)	–	12.6±1.7
Daily toothbrushing (%)		
Once	29	58
Twice	71	42

Table 2. Location, position, and stability of dental implants at baseline and at 3 months. Means of the resonance frequency analysis (RFA) are expressed in implant stability quotient (ISQ).

Groups	Location of implants (n)		Position of fixture (n)		RFA (ISQ) (mean ± SD)		
	Maxilla	Mandible	Submerged	Non-submerged	Immediate implant stability	Implant stability at 3 months	p-value**
Non-diabetic	30	29	31	26	77.48 ± 6.0	79.75 ± 5.5	0.11
Type 2 diabetes	28	31	29	32	75.79 ± 6.6	79.06 ± 6.0	0.008***
p-value*					0.31	0.64	

ᔆBetween-group p-value; **Within-group p-value; ***Denotes statistically significant p-value obtained by the Mann-Whitney U test.

Table 3. Peri-implant bone loss in T2DM and NT2DM at 1, 2, 3, and 7 years.

Groups	PIBL (mm)			
	At 1 year	At 2 years	At 3 years	At 7 years
Non-diabetic	0.23 ± 0.28	0.33 ± 0.46	0.41 ± 0.57	0.58 ± 0.70
Type 2 diabetes	0.53 ± 0.55	0.74 ± 0.62	0.91 ± 0.73	1.1 ± 0.81
p-value	0.004*	0.004*	0.002*	0.00*

*Denotes statistically significant p-value obtained by the Mann-Whitney U test.

Table 4. Peri-implant bone loss in submerged and non-submerged dental implants at 1, 2, 3, and 7 years.

Groups	PIBL (mm)			
	At 1 year	At 2 years	At 3 years	At 7 years
Non-diabetic				
Submerged implants	0.22 ± 0.36	0.34 ± 0.52	0.41 ± 0.71	0.71 ± 0.74
Non-submerged implants	0.28 ± 0.17	0.51 ± 0.34	0.62 ± 0.31	0.95 ± 0.57
Type 2 diabetes				
Submerged implants	0.33 ± 0.36	0.36 ± 0.43	0.44 ± 0.62	0.76 ± 0.76
Non-submerged implants	0.34 ± 0.50	0.63 ± 0.56	0.82 ± 0.63	1.07 ± 0.76
p-value				
Submerged implants	0.026	0.075	0.069	0.055
Non-submerged implants	0.014	0.022	0.024	0.005

P-values in boldface indicate statistical significance (p < 0.05) between both groups

who need dental implants. Some T2DM patients fail to control their glucose levels and maintain mean HbA1c values between 8.5% and 9%.[17] This study analyzed peri-implant marginal bone loss in diabetic and non-diabetic individuals. The findings of the present observational study concur with those of several earlier studies, which demonstrated that hyperglycemic state leads to alterations in bone functions.[18,19,20,21] Other retrospective studies have also recognized pathological changes in bone function related to chronic hyperglycemia.[22,23] The present study observed that PIBL was high in T2DM patients in relation to mean HbA1c levels of 8.2%. These results corroborate those of previous clinical studies that showed increased alveolar bone loss among T2DM patients compared with non-diabetic individuals.[24,25] This pathological mechanism can be explained by the increased serum levels of destructive proinflammatory cytokines (such as interleukin [IL]-1β, IL-6, and tumor necrosis factor alpha [TNF-a]) and of peri-implant crevicular fluid, as a result of the increased production of AGEs and impairment of the chemotactic and phagocytic functions of polymorphonuclear leukocytes in T2DM patients.[26,27]

High expression of proinflammatory cytokines has been observed in bone tissue, supporting the idea that the bone itself produces an inflammatory response in T2DM patients.[28] Mechanisms of this type are likely

to induce osteoclast formation and bone destruction, which may explain bone loss around implants of T2DM patients in the present study.[29,30] However, increased bone resorption was statistically significant at 1, 2, 3, and 7 years, a finding that is consistent with Morris et al.[31] and Gómez-Moreno et al.,[32] whose T2DM patients showed high bone resorption rates during the progression of the disease according to the evaluation of implant survival rate or mean peri-implant bone level measured radiographically.

Interestingly, alveolar bone loss was observed around submerged and non-submerged implants in both groups. Clinically, however, the most important finding in this study was the significant osseous changes around non-submerged dental implants in T2DM and NT2DM patients. The exact mechanism that underlies peri-implant bone changes around non-submerged dental implants is not known. However, several possibilities could explain these findings. One mechanism may involve bacterial colonization in the microgap and implant components. Evidence has been published which demonstrates the presence of bacteria in these areas under certain conditions.[33,34] The epithelium could migrate beyond the microgap in an attempt to isolate the infection. This epithelial proliferation and subsequent physiological response to establish a biological width could be responsible for the approximately 1 mm of distance observed apically to the microgap. Moreover, another important factor that governs PIBL is daily oral care at home. Twice-daily toothbrushing was reported by 71% of NT2DM patients. However, only 42% of T2DM patients performed twice-daily toothbrushing. Therefore, plaque build-up as a result of low toothbrushing frequency may have contributed towards increased PIBL among T2DM patients.

The main strength of the present study is the study design and the follow-up period. No study has assessed PIBL around submerged and non-submerged dental implants in T2DM and NT2DM patients using a 7-year follow-up. Nevertheless, this study certainly has some limitations that should be taken into consideration when evaluating the present findings. First, there was no stratification of HbA1c levels among T2DM patients, and glucose levels were simply presented as a single mean value for all T2DM individuals. Furthermore, other peri-implant clinical parameters, such as peri-implant probing depth, should also have been assessed in order for PIBL to be deemed pathological. In addition, future observational studies should focus on the collection of peri-implant crevicular fluid to quantify the levels of cytokines at the sites of bone loss in T2DM patients. Moreover, cross-sectional studies should be performed for qualitative assessment of microbial plaque around dental implants in T2DM and NT2DM patients.

Conclusion

In conclusion, the results of the present 7-year follow-up clinical study demonstrated significant PIBL around non-submerged single-tooth implant-supported restorations in T2DM as compared to NT2DM patients, which may be explained by the immune inflammatory status of diabetic patients.

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