Role of Peri-implant Clinical Parameters in Change of Blood Glucose Level on Type 2 Diabetes Mellitus: A Literature Review

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Abstract

Purpose: With the increasing use of implant therapy in patients with type 2 diabetes mellitus (T2DM), it is essential to regularly assess the peri-implant condition by observing the changes in clinical parameters such as probing depth (PD), bleeding on probing (BOP), and marginal bone loss (MBL). Studies have shown parameters may change with increasing glycated hemoglobin (HbA1C) levels; thus, comparison of changes in variables may preliminarily predict the progression of plasma glucose level, which is meaningful for the guidance of clinical prevention.

Materials and methods: An electronic search was conducted in three databases up to and including March 2016. Two independent reviewers selected literature, performed quality assessment by utilizing the Newcastle-Ottawa scale (NOS) in which PD, BOP, MBL were used to evaluate the peri-implant condition.

Results: A total of 8 prospective studies were included, which had low risk of bias by NOS. Parameters increased in relation to HbA1C level. In the moderately and poorly controlled diabetes groups, BOP and MBL increased significantly, while PD did not. If PD reaches 2.75 mm, BOP is above 0.65, MBL increases to 1.03 mm or progresses to peri-implantitis, (especially with clear increases in BOP and MBL), blood glucose levels may not be controlled in T2DM patients.

Conclusion: On the premise of well-controlled oral hygiene maintenance, this result suggested the interrelation between clinical parameters and blood glucose level, observing the peri-implant condition could contribute to suggest the need for further instructions of blood glucose levels in patients with T2DM.

Key Words: Peri-implantitis, HbA1C, Type 2 diabetes mellitus, Blood glucose, Probing depth, Bleeding on probing, Marginal bone loss

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic systemic disease with an annually increasing incidence. According to the newly-released 7th edition of the Diabetes Atlas from the International Diabetes Federation (IDF), about 415 million people were estimated as having diabetes worldwide in 2015, a number that is expected to grow to over 642 million by 2040 [1] . Patients with T2DM are more likely to develop periodontitis, which leads to periodontal attachment and tooth loss over time. Even more serious is the loss of chewing function, which significantly impacts the quality of life.

Dental implant therapy is a mature dental rehabilitation treatment for partial or total edentulism. The dental implant therapies have been shown to be safe, with high success rates. However, diabetes remains a relative contraindication for implant therapy that depends on the glycemic control [2]. Hyperglycemia can cause delayed healing, infection, and cardiovascular complications. A number of studies have shown that patients with well-controlled glycemic levels can successfully undergo implant therapy [3-5], and several studies have demonstrated that patients with poorly controlled glycemic level may also be candidates for implant treatment [6-8]. Glycosylated hemoglobin levels (HbA1C) can indirectly reflect the mean blood glucose levels over the previous 2-3 months [9]. Therefore, HbA1C levels can be used as a diagnostic criterion to assess the severity of DM.

Patients with diabetes are generating a great demand for implant therapy; hence, regular checks of the peri-implant condition are very important. The state of peri-implant health (peri-implant mucositis or peri-implantitis) [10] can be characterized by several variables, including probing depth (PD), bleeding on probing (BOP), and marginal bone loss (MBL) [11]. These parameters differ with varying HbA1C levels; thus, we hypothesized that changes in these parameters may predict the progression of plasma glucose levels. For community dentists whose patients undergo implant therapy and return for examination, evaluation of these parameters in the area around implant allows assessment of the peri-implant status due to its direct view. Comparison of peri-implant conditions permits dentists a preliminary assessment of blood glucose levels. Few studies have focused on the variations in parameters with reference to varying HbA1C levels. This review evaluated the relationships between changes in PD, BOP, MBL, and increased glycemic levels in order to determine their usefulness to estimate HbA1C levels and to provide guidance for clinical applications.

Material and Methods

Search strategy

Searches were performed independently by two reviewers. An electronic search was performed including papers published up to and including March 2016 in the MEDLINE-PubMed database, Web of science and Cochrane library. The following search strategy with different combinations was used to explore the databases: dental or oral implant, type-2 diabetes mellitus, diabetic, HbA1C, peri-implant, clinical parameters.

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Inclusion criteria

The included studies were published in English.

Case-control studies, prospective cohort, and retrospective studies were included in the study.

The studies were required to have a control group (for diabetic patients, a healthy without diabetes group was setted)

The studies had at least six months follow-up.

Studies were excluded if they were animal or experiential studies or if they used inadequate clinical parameters (PD, BOP, MBL not mentioned). Review articles were excluded.

Quality assessment

The studies included in this review were performed based on the Newcastle-Ottawa Scale (NOS) by two independent reviews. The NOS [12] was utilized to assess the prospective or retrospective studies. The scores ranged from 0 (high risk of bias) to 9 (low risk of bias).The criteria were as follows: selection, comparability, outcome. The selection has four items: representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure, demonstration that outcome of interest was not present at start of study. Comparability has one item: comparability of cohorts on the basis of the design or analysis. Outcome has three items: assessment of outcome was follow-up long enough for outcomes to occur, adequacy of follow up of cohorts. A study can be awarded a maximum of one star for each item within the selection and outcome categories. A maximum of two stars can be given for comparability.

Data Extraction

Data were extracted by two reviewers, who read the literature to identify the data. The information extracted from the included studies included author, year of publication, methods, participant characteristics (age, smoking status, duration of type-2 diabetes in years), preoperative and postoperative data, and evaluation of the clinical parameters. Disagreements in the included studies were resolved by discussion.

Results

Search results

The electronic search revealed a total of 118 articles; after reviewing the titles and abstracts, 18 studies were identified. Of these, 10 were excluded: five due a lack of clinical parameters [7, 8, 13-15], three due no control group [6, 16, 17], and two systemic reviews [18, 19]. Finally, eight full-text articles were included in the analyses (*Figure 1*). The Kappa values for agreement of the included studies were 0.80. The eight studies were prospective studies [4, 5, 9, 20-24].

Quality assessment

None of the studies gained the maximum score, all of the studies gained the maximum score in the selection item, two of the studies [22, 24] had no score in the comparability item, one of the studies [9] gained maximum score in the outcome item. In summary, most of the studies have a medium quality, only one study [22] has a low quality (*Table 1*).

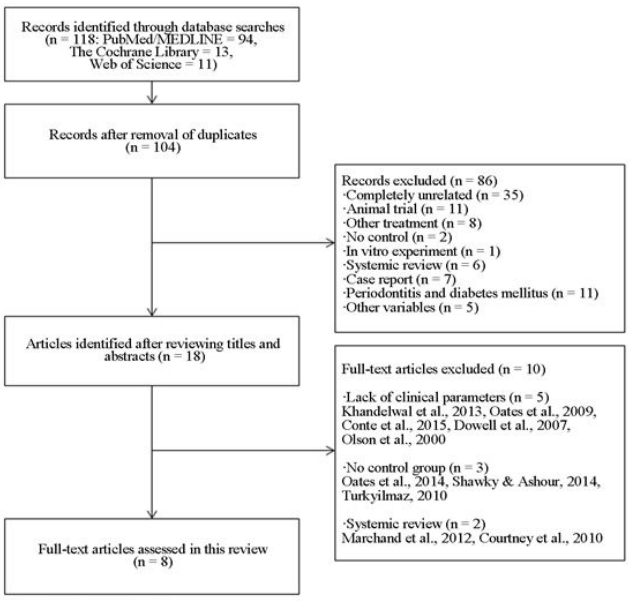

Figure 1. *Search strategy flowchart.*

Study descriptions

The main characteristics of the studies are described in *Table 2*. The studies enrolled participants between 40 and 60 years of age. Among the included studies, one [4] had a seven-month follow-up, observing the clinical parameters and levels of proinflammatory cytokines in the crevicular fluid, plaque index (PI), gingival index (GI), BOP, PD, clinical attachment level (CAL) at one, four, and seven months, while MBL was measured only in the test group. Two of the studies had one-year follow-ups; Tatarakis et al. [5] described the clinical, microbiological, and salivary biomarker profiles, as well as PD, CAL, BOP, and PI and radiograph bone level (RBL). Erdogan et al. [22] measured guided bone regeneration, MBL, and resonance frequency analysis (RFA). Three studies had two-year follow-ups: Al Amri et al. [20] described platform-switched implants and did not use bone regeneration. BOP and PD were described in box plots, and only MBL was described as means ± standard deviation (SD). Another study from Al Amri et al. [21] reported on the changes in clinical parameters with the oral hygiene maintenance. Aguilar et al. [9] immediately loaded implants in esthetic zone and measured PD, BOP, and MBL within six months and one and two years. One study each [23, 24] had three-year 12-year follow-ups, respectively. MBL was measured by periapical radiographs. Only four studies [9, 21, 23, 24] had patients with moderately or poorly controlled diabetes; the others classified patients into two groups, without diabetes or with well-controlled diabetes.

Changes in clinical parameters and HbA1C

Aguilar et al. [9] showed that higher HbA1C levels were associated with a decrease in implant survival rate from 100% to 86.3%. The MBL was higher in Group 3, (1.92 ± 0.38 mm after two years), compared to Group 2 (0.98 ± 0.27 mm) and

Group 1 (0.72 ± 0.27 mm). The PD was greater in Group 3, reaching 3.43 ± 0.23 mm.

Table 1. Risk bias of included studies.

Item	Aguilar et al, 2016[9]	Aguilar et al, 2016[9]	AL Amri et al, 2016[21]	Dogan et al, 2015[4]	Erdogan et al, 2015[22]	Gomez et al, 2015[23]	Tatarakis et al, 2014[5]	Tawil et al, 2008[24]
Selection	****	****	****	****	****	****	****	****
Comparability	*	*	*	*	-	*	*	-
Outcome	**	*	*	*	*	*	*	***
Total scores	7	6	6	6	5	6	6	7
* awarded 1 point								
- awarded zero point								
Studies less than 6 points were consider to be of low quality, medium quality if having 6 to 7 points while studies had 8 or 9 points were consider to be of high quality.								

Table 2. Main characteristics of the included studies.

Study	Methods	Number of participants[a]	Ages (years)[b]	Implants	Smoking	DM duration (years)	Evaluated parametersc	Preoperative and postoperative management
Aguliar et al, 2016[9]	Immediately loaded implants in the esthetic zone, two-year prospective follow-up study	a: 33 b: 30	a. 59 ± 2.3 b. 57 ± 3.8	85		NR	PD0 MBL, BOP1	postoperative: full-mouth wash, amoxicillin
Al Amri et al, 2016[20]	Delayed loading mandibular implants, two-year longitudinal study	a: 22 b: 23	a. 41.8 (mean) b. 42.4 (mean)	45	NO	14.5±0.7	PD, BOP, MBL:0	preoperative: full-mouth scaling, amoxicillin;postoperative: oral hygiene maintenance
Al Amri et al, 2016[21]	Immediately loaded maxillary implants, two-year follow-up study	a: 30 b: 30 c: 31	a. 48.5 (mean) b. 50.1(mean) c. 50.5 (mean)	91	NO	NR	PD, BOP, MBL:0	six monthly oral hygiene maintenance
Dogan et al, 2015[4]	Delayed loading, seven-month follow-up study	a: 7 b: 13	a. 52.14 ± 3.93 b. 53.54 ± 4.01	39	NR	NR	PD, BOP, MBL:0	preoperative: antibiotic; postoperative: mouthwash
Erdogan et al, 2015[22]	With guided bone regeneration, delayed loading, one-year prospective control study	a: 12 b: 12	a. 49.5 ± 9.3 b. 52.6 ± 7.3	43		At least 5	PD, BOP, MBL:0	preoperative: antibiotic
Gomez et al, 2015[23]	Implants placed in the anterior zone of the maxilla, three-year follow-up study	a: 21 b: 24 c: 11 d: 11	a. 60 ± 7.2 b. 59 ± 8.1 c. 62 ± 6.8 d. 64 ± 5.6	67	NO	NR	MBL,BOP: 1; PD: 0	postoperative: amoxicillin, full-mouth wash
Tatarakis et al, 2014[5]	Implants placed in the anterior regions, one-year cohort study	a: 18 b: 14	a. 64 ± 8.1 b. 65 ± 8.9	At least 32	NR	NR	PD,CAL,BOP,PI, RBL: 0	NR
Tawil et al, 2008[24]	Conventional and advanced implant treatment, 12-year prospective study	a: 45 b: 45	a. 59.6 (mean) b. 64.7 (mean)	499	NO	12.7 ± 11.3	PD:0, BOP, PI, MBL:1	preoperative: control of periodontal disease, antibiotic; postoperative: mouth wash
[a] Number of participants with varying HbA1C levels: a. HbA1C ≤6, b. HbA1C 6.1-8, c. HbA1C 8.1-10, d. HbA1C ≥10.1; [b] Subject ages presented as mean ± standard deviation (M ± SD). a. HbA1C ≤6, b. HbA1C 6.1-8, c. HbA1C 8.1-10, d. HbA1C ≥10.1; [c] The evaluation of peri-implant condition using clinical parameters: PD, probing depth; BOP, bleeding on probing; MBL, marginal bone loss; PI, plaque index; CAL, clinical attachment loss; RBL, radiograph bone loss. The parameters no significant difference between the groups (0) and valuable difference with varying HbA1C levels (1). NR, not reported.								

Similarly, the BOP in Group 3 was 0.74 ± 0.05 mm, compared to 0.44 ± 0.07 mm in Group 1. According to the previous literature [10], peri-implantitis is defined as PD greater than 3 mm and bone loss ranging from 1.8 to 3 mm; thus, the patients in Group 3 were considered to have peri-implantitis. Al Amri et al. [20] found no significant differences in peri-implant BOP and PD between non-diabetic and well-controlled diabetic groups. There were also no significant differences in MBL between the two groups (0.2 ± 0.04 and 0.23 ± 0.08 mm) after two years. Another study also by Al Amri et al. [21] reported that HbA1C levels were significantly decreased at two years compared to those at 6 months in Group 2 (well-controlled group) and Group 3 (moderately controlled group). BOP, PD, and MBL were higher in Group 3 as compared to Group 1 (control group). In Group 3, BOP and PD decreased during the observation period, a change that was attributed to oral hygiene maintenance. In the study by Dogan et al. [4] the alveolar bone levels decreased significantly more in the diabetic group and had increased HbA1C levels, although no difference were found between the groups, a finding similar to those of the studies by Tatarakis et al. [5] and Erdogan et al. [22]. Gomez et al. [23] also reported that MBL and BOP increased in relation to increased HbA1C levels, while PD did not differ between the groups. This finding is in accordance with those by Tawil et al. [24], who reported no difference in PD between groups, while the MBL reached 1.62 mm with increasing HbA1C levels.

Average clinical parameters at one and two years according to HbA1C levels

Tables 3-5 show the average PD, BOP, and MBL. At one year, the mean PD around the implants was lower (2.22 mm) for HbA1C levels ≤6 compared to 2.39 mm for HbA1C 6.1-8 and 2.75 mm for HbA1C 8.1-10. The BOP and MBL increased to 0.62 and 0.87 mm (HbA1C 8.1-10), respectively, compared to the well-controlled diabetes groups (0.56 and 0.45 mm, respectively) and non-diabetes groups (0.63 and 0.53 mm, respectively). Similarly, at two years, the mean PD increased with HbA1C levels. BOP and PD showed the same tendency. At one and two years, fluctuating range was not relatively great. Although most studies showed that there were no significant differences between the non-diabetes and well-controlled diabetes groups, a visible increase was observed.

Taken together, the parameters increased in relation to HbA1C level, especially for HbA1C levels above 8. Based on these observations, PD above 2.39 mm, BOP higher than 0.56, and MBL over 0.63 mm may indicate HbA1C levels above 6. Similarly, a PD increase to 2.75 mm, BOP above 0.65, and MBL increase to 1.03 mm suggests uncontrolled blood glucose levels in T2DM patients.

Table 3. Average probing depths (PDs) at one and two years according to HbA1C levels

	PD (1 year)			PD (2 years)		
	HbA1C ≤6	**HbA1C 6.1-8**	**HbA1C 8.1-10**	**HbA1C ≤6**	**HbA1C 6.1-8**	**HbA1C 8.1-10**
Aguilar et al, 2016[9]	2.6	2.66	3.57	2.67	2.79	3.68
AL Amri et al, 2016[21]	1.9	2.3	2.4	1.6	2.3	2.3
Gomez et al, 2015[23]	2.19	2.24	2.29	2.21	2.27	2.31
Tatarakis et al, 2014[5]	2.2	2.35	-	-	-	-
Average	2.22	2.39	2.75	2.16	2.45	2.76
- not mentioned in the study						

Table 4. Average bleeding on probing (BOP) at one and two years according to HbA1C levels

	BOP (1 year)			BOP (2 years)		
	HbA1C ≤6	**HbA1C 6.1-8**	**HbA1C 8.1-10**	**HbA1C ≤6**	**HbA1C 6.1-8**	**HbA1C 8.1-10**
Aguilar et al, 2016[9]	0.39	0.45	0.65	0.44	0.51	0.74
AL Amri et al, 2016[21]	0.4	0.6	0.63	0.4	0.62	0.62
Gomez et al, 2015[23]	0.43	0.52	0.59	0.47	0.54	0.6
Tatarakis et al, 2014[5]	0.56	0.67	-	-	-	-
Average	0.45	0.56	0.62	0.44	0.56	0.65
- not mentioned in the study						

Table 5. Average marginal bone loss (MBL) at one and two years according to HbA1C levels

	MBL (1 year)			MBL (2 years)		
	HbA1C ≤6	HbA1C 6.1-8	HbA1C 8.1-10	HbA1C ≤6	HbA1C 6.1-8	HbA1C 8.1-10
Aguilar et al, 2016[9]	0.64	0.86	1.54	0.72	0.98	1.92
AL Amri et al, 2016[20]	0.22	0.18	-	0.23	0.2	-
Gomez et al, 2015[23]	0.41	0.45	0.51	0.48	0.52	0.59
AL Amri et al, 2016[21]	0.45	0.54	0.57	0.46	0.58	0.59
Erdogan et al, 2015[22]	0.93	1.13	-	-	-	-
Average	0.53	0.63	0.87	0.47	0.57	1.03
- not mentioned in the study						

Discussion

The aim of this review was to evaluate the changes in the clinical parameters of peri-implant tissues in T2DM patients with different glycemic levels, as measured by HbA1C. Several variables were selected in order to assess peri-implant health; of these, periodontal probing is the most important method to check the periodontal state. The PD reflects the attachment level. Bleeding on probing around the implant indicates whether there is mucositis. Radiographs are used to evaluate bone loss and the severity of peri-implantitis. Plaque index (PI) reflects oral hygiene. Gingival index (GI) indicates the gingival condition based on the presence of inflammation. Clinical attachment level (CAL) reflects the severity of attachment loss. As clinical parameters such as PI, GI, and CAL are described in few studies, this review selected the common variables PD, BOP, MBL to evaluate the state of the peri-implant tissue in T2DM [10].

The results of the present review showed that PD was not useful for the evaluation of peri-implant state, a finding that may be explained by the fact that the PD around implants is influenced by a variety of factors such as the profile of the abutments and the mucosal thickness [25]. In this review, four studies [9,20,21,23] mentioned that each patient received one-piece implants in order to avoid the influence of prosthetic designs. Hence, probing may not exactly reflect the peri-implant condition in diabetic patients to evaluate for the progression of diabetes. However, probing is an essential tool for the diagnosis of peri-implant disease. Studies have shown that probing is useful to estimate implant bone loss [11, 25]. The clinical parameter BOP increased with increasing HbA1C levels and is, therefore, a useful parameter to evaluate the peri-implant condition [11]. In turn, it may be valuable to predict the progression of diabetic patients by comparing the changes over study periods. MBL is a useful tool to diagnose peri-implantitis [10]. MBL increased in relation to higher HbA1C levels; it is therefore possible that assessment of the changes in MBL may benefit people with diabetes by allowing evaluation of the disease severity. Therefore, comparison of the changes in clinical parameters allows us to predict the recent changes in blood glucose, which permits further patient instruction on the control of blood glucose levels. In this review, there were no differences in parameters in patients with well-controlled plasma glucose levels, a finding in concordance with most studies that patients with well-controlled diabetes can undergo implant therapy. However, these patients should pay attention to their blood glucose levels, as these parameters are all elevated compared to the normal population. When PD increased to 2.76 mm, BOP increased to 0.65, and the MBL was higher than 1.03 mm, or even developed to peri-implantitis, blood glucose levels may be moderately or poorly controlled; dentists should make patients aware of this, combined with checking blood glucose levels, and remind patients to control their glycemia. In summary, when T2DM patients finish implant therapy and return for a check-up after one year, dentists can preliminarily assess their blood glucose level by evaluating the changes in these clinical parameters and provide guidance for patients to take measures to control their blood glucose levels. Few studies have used clinical parameters to evaluate the peri-implant condition in patients with diabetes, or the parameter data are not complete. However, the implant procedures differed in each of the included studies. Two studies [9, 21] immediately loaded, while others delayed loading. One study compared traditional and advanced implant treatments [24]; implant loading different, one study in mandibular [20], some in maxillary [5,9,20,22,23]; and two studies [22,24] used guided bone generation. These differences can influence the clinical parameters. The results of this review underscore the importance of oral hygiene maintenance [21] before and after implant surgery, including measures such as full-mouth scaling using chlorhexidine, antibiotic use [26], and minimizing periodontal infections. These measures will increase the success rate in patients with diabetes. The findings of the present review suggest that glycemic levels might be out of control when the peri-implant condition develops to peri-implantitis; thus, it is important for community dentists to evaluate the change of blood glucose level further to guide patients to control of their blood glucose levels.

Conclusion

On the premise of well-controlled oral hygiene maintenance, increases in clinical parameters, especially BOP and MBL, may be valuable for evaluation of the peri-implant conditions. PD above 2.39 mm, BOP higher than 0.56, and MBL over 0.63 mm might indicate HbA1C levels above 6. When the PD

reaches 2.75 mm, the BOP is above 0.65, and the MBL increases to 1.03 mm or to peri-implantitis, blood glucose levels might be uncontrolled in T2DM patients, indicating that community dentists should monitor blood glucose changes and recommend patients take measures to control their blood glucose levels. Although the present clinical data is limited, however, it is a hint that with the increasing clinical parameters, the risk of blood glucose change also rises. Further studies with complete clinical parameters should be conducted in order to fully investigate the associations.

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