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Implant loss in Diabetic Patients: A Systematic Review

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ABSTRACT

The aim of this systematic review to evaluate the effect of diabetes on dental implants loss .Review authors searched 3 electronic databases; Pubmed, Cochrane and Lilacs: 11/10/2018, hand searched 11 journals till November 2018 and snowballing: 15/10/2018. Adult female and male patients above 18 years old, either completely or partially edentulous, maxillary and/or mandibular dental implants, restored by fixed or removable prosthesis, were included. Surgical modifications, drugs that affect bone density, like vitamin D and biphosphonates, were excluded. Diabetic patients, who are classified either controlled or uncontrolled were considered eligible. Review authors extracted data relevant to PECOT. Data was descriptively and statistically analyzed. 14 studies; 9 prospective and 5 retrospective studies, involving 1398 participants and 3282 implants, were included in this systematic review. 3 studies were included in the meta-analysis. Based on the results of implant loss 2 years following implant placement, implant therapy in diabetic patients seems to be possible. However, results should be taken with extreme cautions, since the quality of evidence is very low.

Keywords: Diabetes mellitus, high blood sugar, Dental implants, Oral implants

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INTRODUCTION

Diabetes mellitus considered as a relative contraindication for dental implants, according to the blood glucose level and the glycosylated hemoglobin (HbA1c). [1,2] The duration of the endocrinal disorder, more than 10 years, is responsible for micro-vascular complications and implant failure [3,4] due to the inhibition of osteoblastic and the promotion of osteoclastic activity.[3] The condition also affects the response of the parathormone hormone, which regulates calcium and phosphate mechanism[5]. Which affects bone matrix formation and decreases growth and formation of extracellular matrix,[5,6] Therefore, bone formation during healing inhibited.

Management of periodontal infection and inflammation was found to be associated with a decrease in the glycosylated hemoglobin level. So, claimed to improve the success rate of dental implants in diabetic patients. [15],[16] In Addition to, the use of wide and long implants that were surface treated by active materials, prophylactic antibiotics post-surgically and 0.12% chlorhexidine mouth rinse twice daily were claimed to improve the survival of implants in diabetic patients. [10,17,18] The chlorhexidine mouth rinse was found to be effective in decreasing the effect of P. gingivalis infections and peri-implant mucositis.[19,20,21]

Unfortunately, results of available reviews should be taken with caution due to heterogeneity between studies, populations, un managed confounders and increased risk of bias. absence of SRs with only the inclusion of controlled and randomized clinical trials with accurate calculation of the sample size should be undertaken. In addition, better interpretation of the data would be possible if the studies included questions such as type of implant, location of the implant, type and duration of diabetes, glycemic control, and type of prosthetic restoration. So, this systematic review (SR) aims to explore whether dental implant placement in well or uncontrolled diabetic patients, if compared to healthy subjects increases the risk of implant failure.

MATERIALS AND METHOD

This SR was reported following the PRISMA7[23] (preferred reporting items for systematic reviews and meta-analysis) statement. The review was registered at Removable Prosthodontics Department, Faculty of Oral and Dental Medicine, Cairo University.

Selection Criteria

Adult female and male patients above 18 years old, completely or partially edentulous, maxillary and/or mandibular dental implants, restored by fixed or removable prosthesis, were included. Surgical modifications, drugs that may affects bone density, like vitamin D and biphosphonates, were excluded. Diabetic patients, who are classified either controlled or uncontrolled were considered eligible. Cohort studies, randomized and non-randomized

clinical trials, comparing between implants in diabetic and non-diabetic patients were included. Articles reporting survival rates as an outcome without referring to the follow up duration were excluded. Reviews, case series, case reports, animal studies, in-vitro, case control, cross sectional studies were excluded. Published articles with no limitation for years were considered eligible for this review. Only articles published in English language were included .

Search Methodology

IR, NN and MK searched 3 databases: PubMed, Cochrane and LILACS till October 2018. Detailed search strategy can be seen in Appendix 1 (Supplementary material). Search terms and strategy developed in Medline (PubMed) database are shown in (Table 1), No filters were used in all databases except English filter in LILACS database. Eleven journals were searched by MK and IR till December 2020, These journals were: (Journal of oral implantology, International journal of prothodontics, Journal of clinical implantology researches, European journal of oral implantlogy, International journal of periodontics and restorative dentistry, Journal of clinical oral implants researches, International Journal of Oral & Maxillofacial Implants**,** Journal of Prosthetic Dentistry**,** Quintessence International ,Journal of dental researches and journal of oral and maxilla-facial surgery). Reference lists of eligible articles and previously published systematic reviews were also screened by M.K. and IR to make sure no articles were missed during the search. During the selection process 23 authors were contacted about missing data.

Table 1: Search strategy.

Exposure	Population
dental implant	diabetes mellitus
dental implants	type I diabetes
Oral implant	type II diabetes
Oral implants	1diabetes
Osseointegrated implants	2diabetes
Osseointegrated implant	2diabetes mellitus
Dental implant osseointegration	Diabetic patient
dental implanting	Diabetic patients
oral implanting	Elevated blood glucose
Dental implantology	Hyperglycemia
Oral implantology	Hyperglycaemia
Oral implantation	High blood glucose
Implant prosthodontics	diabetes blood glucose
Implant prostheses	blood sugar diabetes
Fixture	High blood sugar
Fixtures	

Table 2: Methodological Characteristics of Included Articles

Study ID	Exposure				Sample size							Drop-outs				
	ND	D			Final in SR											
		CD	UCDM		Total	ND	D				Mixed ND/CD (ADA)	ND	WC	MC	PC	Management of failed & lost in SR
			MC	PC			CD	UCDM		Total						
								MC	PC							
Al Zahrani 2018 A[69]	HbA1c ≤6	>6-8.2	-	-	70	35	35	-	-	35	-	0	0	0	0	-
Al Zahrani 2018 B[119]	HbA1c ≤6		HbA1c >8		67	67	35	32		67	-	0	0	0	0	-
Eskow 2017[120]	-	HbA1c 6-7.9	HbA1c 8-9.9	HbA1c 10-13.9	24	-	9	9	6	24	-	0	4	0	0	4 patients excluded(unknown group)
Ghiraldini 2016[88]	HbA1c <6	HbA1c 6-8	HbA1c > 8 -		51	19	16	16		32	-	1	1	0	0	Not considered in total number (meta-analysis)
Al Amri 2016[121]	HbA1c <6	HbA1c 6.1-8	HbA1c 8.1-10	-	91	30	30	31	-	61	-	0	0	0	0	-
Aguilar 2016[122]	HbA1c ≤6	HbA1c 6.1-8	HbA1c 8.1-10	excluded	85	33	30	22	-	52	-	0	0	0	0	-
Gomez 2015[123]	HbA1c <6	HbA1c 6-8	HbA1c 8-10	HbA1c > 10	67	21	24	11	11	46	-	0	0	0	0	-
Oates 2014[124]	HbA1c <5.9 FPGL≤100	HbA1c 6-8	HbA1c 8-10	HbA1c> 10	117	50	47	20	-	67	-	3	3	1	0	Not considered in total number (meta-analysis)
Tawil 2008(125)		HbA1c ≤ 7.2	HbA1c 7-9	HbA1c >9	90	45	22	22	1	45	22	NR				NR
Total					662	300	248	163	18	429	-	4	8	1	0	

D Diabetic, ND non diabetic, PC poor controlled diabetes, UCDM uncontrolled diabetes mellitus, ADA American Diabetes association classification, CD completely denture, P partially edematous, C completely edematous T total, NA not available , NR not reported

Table 2: Methodological Characteristics of Included Articles

Study ID	Exposure				Sample size							Drop-outs				
	ND	D			Final in SR											
		CD	U-CDM		Total	ND	D				Mixed ND/CD (ADA)	ND	WC	MC	PC	management
			MC	PC			CD	U-DM		Total						
								MC	PC							
Al sahhaf 2019	HbA1c< 6.5 ADA	HbA1C %≥6.5	>8	-	119	40	41	38	-	79		0	0	0	-	
Al sharani 2020	5.6	5.7-6	6-8	8	75	25	25	25	-	50		0	0	0	-	
Mokeem 2018[126]	HbA1c <6 NADA	HbA1c 6-8	HbA1c 8-10	HbA1c > 10	93	26	25	25	17	67	-	0	0	0	0	
Al Sowygh 2018[127]	HbA1c< 6.5 ADA	HbA1C %≥6.5	>8		71	25	22	24	-	46	47	0	0	0	0	
Abduljabbar 2017[128]				HbA1c > 10	130	42	45	-	43	88	87	0	0	0	0	
Bignozzi 2013[129]	HbA1c5.95±0.65 FPGL88.80±2.2	HbA1c9.05±1.07 FPGL132±5.81			30	22				8	22	0	0	0	0	
Alsaadi 2008(130)	FPGL≥126	FPGL≥126			412	402	D II:9 D I: 1			10	-	0	0	0	0	
Total retrospective studies					930	582	158	112	60	348	156					
Total all studie					1592	815	390	243	126	777	178					

D Diabetic, ND non diabetic, PC poor controlled diabetes, UCDM uncontrolled diabetes mellitus, ADA American Diabetes association classification, CD completely denture, P partially edematous, C completely edematous T total, NA not available, NR not reported

Study Selection

All identified studies were imported to (Endnote X7.4) and all duplicates were removed. The titles and abstracts of identified studies were screened by MK and NN independently. Secondary screening was carried out by MAK, NN, and MK through full text. Disagreements were resolved a third review author IR.

Data Collection Process

IR and MK independently and in duplicate extracted the data of included studies using paper-based data extraction forms. Before reading the included studies a preliminary data extraction form, containing information about participants, exposure, comparator, outcomes, time points and study design was used.

Risk of Bias

IR and MK assessed the risk of bias for the included trials independently for all studies. In case of disagreement between both authors, a third reviewer MAK was involved to resolve the issue

Data Analysis

I.R. and M.K. planned to perform a meta-analysis using review manager software (RevMan) Version 5.3. The statistical heterogeneity was assessed by various methods; first eyeballing. IR and MK planned to do subgroup analysis if more than 10 studies were included. However, it was only possible to do subgroup analysis for the level of diabetes.

RESULTS AND DISCUSSION

Figure 1 shows the number of articles identified at the different stages of the review. By searching the electronic databases, 6833 references were retrieved in addition to 101 references identified through hand searching, which resulted in a total of 6934 article. After duplicates removal, title and abstract screening resulted in excluding 6851 records and 79 articles were eligible for full text reading. The latter resulted in the exclusion of 65 articles and the inclusion of 14 articles in this SR. From these articles, 13 were included in the meta-analysis. 9 were prospective and 5 retrospective cohort studies

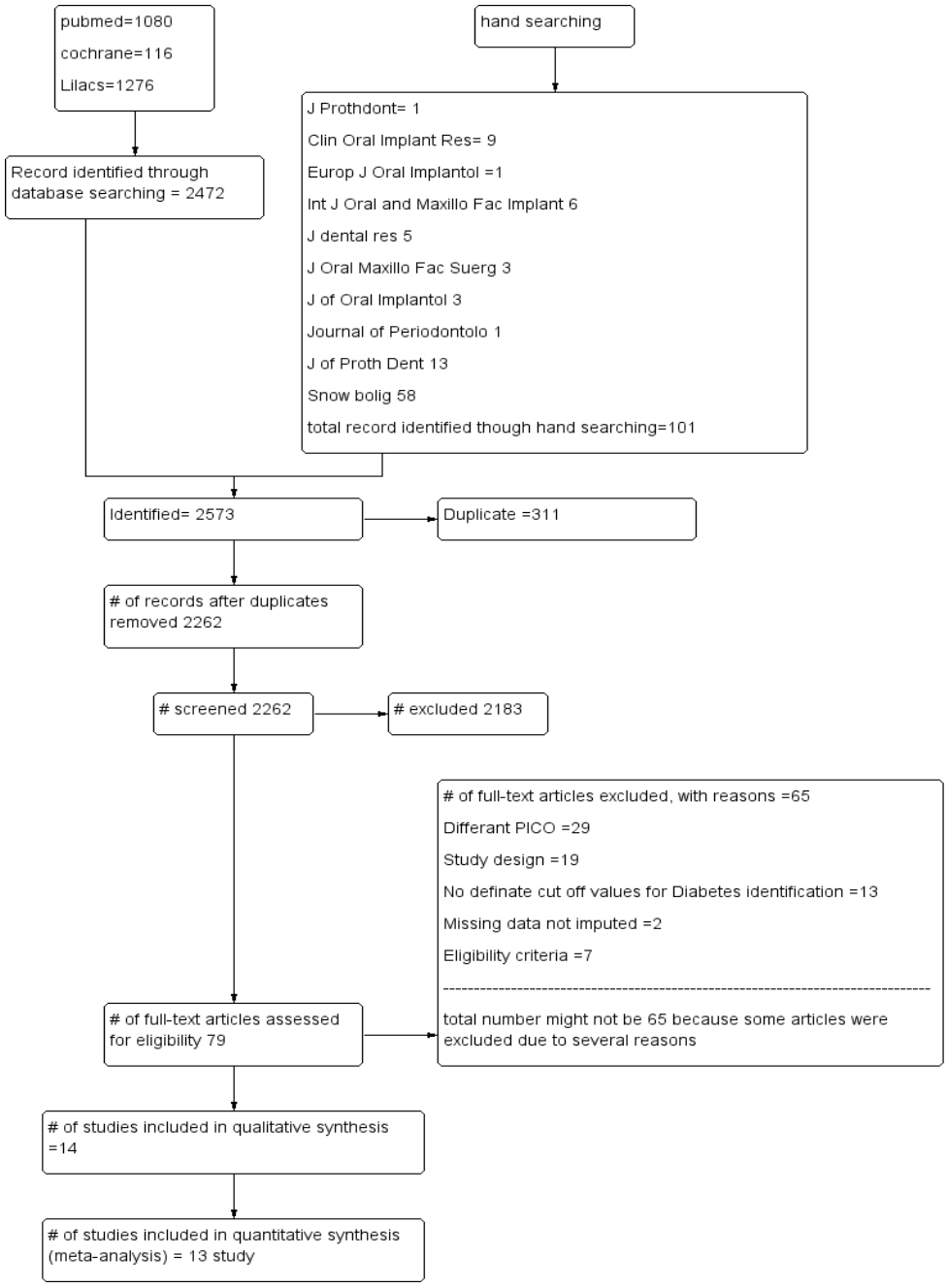

Figure 1: PRISMA Flow diagram indicating number of studies during different review stages.

Description of included studies

A total of 14 studies were identified for inclusion in the review. Number of studies identified through the different stages of the review is clarified in the PRISMA[23] flow diagram (Figures 1).

From the 14 included studies, 7 were performed in KSA [31 ,32 , 33 , 34 , 35 ,36 ,37] , two [38 ,39] in USA, two [40 , 41] in Spain, one [42] in Belgium, one [43] in Greece, one [44] in Brazil, one in Italy [45] and one [46] in Lebanon., 9 were prospective [47, 32 , 38 ,44 ,40 ,34 ,48 , 49 , 46] and 5 retrospective cohort studies[35, 36 ,37, 31, 42]. The female to male ratio was 762/678 (1.12/1). This was based on all of included studies except Abduljabbar 2016[31], who did not report the gender distribution in

their study. Age of patients ranged between 29 to 85 years, with a mean age of all 54.89 years, that was calculated based on all studies except Al Saadi 2008[42], who did not report the mean age of their participants. The duration of the endocrinal disorder was not reported in 6 studies [34,48,49,40 45,42]. The mean duration of diabetes mellitus in years was 7.13 years based on the studies that reported the mean duration. The minimum duration for implants in function was 12 months and the maximum was 144 months, with a mean duration of 45.499 months, 38.04 months for the prospective studies and 52.954 months for the retrospective ones.

A total of 3282 implants were inserted in 1398 participants; 2213 non-diabetic and 1069 diabetic patients, The participants were partially edentulous patients with multiple missing teeth in 5 studies.[38,44,35,31,49,] 2213 implants were placed in non-diabetic, while 1069 implants were placed in diabetic ones, where 493 were placed in the well, 364 in the moderately and 178 in the poorly controlled diabetic patients. while the study of Oates 2014[49] included completely edentulous patients only. Five studies[47,32],[34,48,36] included patients with single missing tooth. The remaining four studies[46 43,45,42] did not report the edentulous status. The condition of the opposing dentition was not reported in all studies except Oates 2014[49] which included completely edentulous arches and Gomez 2015 which included opposing natural dentition. The ratio of implants placed in the maxilla to the mandible is 1:1.26. The duration of the endocrinal disorder was not reported in 6 studies [34,48,49,40 45,42]. The mean duration of diabetes mellitus in years was 7.13 years based on the studies that reported the mean duration. The minimum duration for implants in function was 12 months and the maximum was 144 months, with a mean duration of 45.499 months, 38.04 months for the prospective studies and 52.954 months for the retrospective ones.

Risk of bias assessment

Figure 2 shows the review author's judgments about each risk of bias assessment for each domain for each of the included studies. 8 studies were judged at critical risk of bias and 6 at serious risk of bias

Quantitative Analysis

9 studies reported implant loss as an outcome, all of them showed no significant difference between patients with higher and lower HbAc1. Results were considered significant at $P \leq .05$. This SR included a meta-analysis showing the results of implant loss at 24 months following implant insertion. The results showed no significant difference in the comparison of diabetic and healthy patients with RR 1.1[0.37, 3.26], P=.86, heterogeneity $T^2= 0$, $I^2 = 0\%$, after 6 months, RR = 1.35[0.62, 2.95], P= .45, heterogeneity $T^2= 0$ $I^2 = 0\%$, after 12 months, RR =1.44[0.35, 5.89] P=.61 45 heterogeneity $T^2= 0.53$ $I^2 = 24\%$ after 24 months, RR 2.27[0.38, 13.53] P=.37 heterogeneity $T^2= 0.55$ $I^2 = 26\%$ after 60 months.

In the comparison between well controlled diabetic and healthy patients, the results revealed no significant difference throughout the whole follow up period with RR =1.8[0.53,6.17], P=.35 heterogeneity T^2= 0 I^2 = 5% after 24 months.

Similarly, in the comparison between moderately controlled diabetic and healthy patients the results revealed no significant difference throughout the whole follow up period at RR =2.41[0.12, 48.34] P=.56, heterogeneity T^2= 2.27 I^2 = 48% after 24 months.

No significant difference was found between the studied subgroups; well and moderately controlled patients as revealed by the p values = 94 at 24 months follow up periods. It was also shown that the results are not sensitive to combining the different levels of the HbAc1 and reporting them separately.

Table 3: Results of implant loss 2 years

	24 months					
	ND	Diabetic				
		WC	Un-CD			P
			MD	PC	TUNC	
	AR	AR	AR	AR		
Al zahrani A 2018	0/59	1/59				
Al zahrani B 2018	1/74		0/50			
Ghiraldini 2016						
Eskow 2017		0/21	1/17	1/21	2/38	
Aguilar 2016	0/33	1/30	3/22			
Oates 2014						
Bignozzi 2013	0/51		0/17			
Tawil 2008	2/244	6/255				
Alsaadi 2008	101/1481	0/33				

ND non diabetic, WC well controlled diabetic, MC moderately controlled, PC poor control, AR absolute risk, T total and Un-CD uncontrolled diabetic, P P-value, AR abs olute risk, green prospective studies and Pink retrospective studies

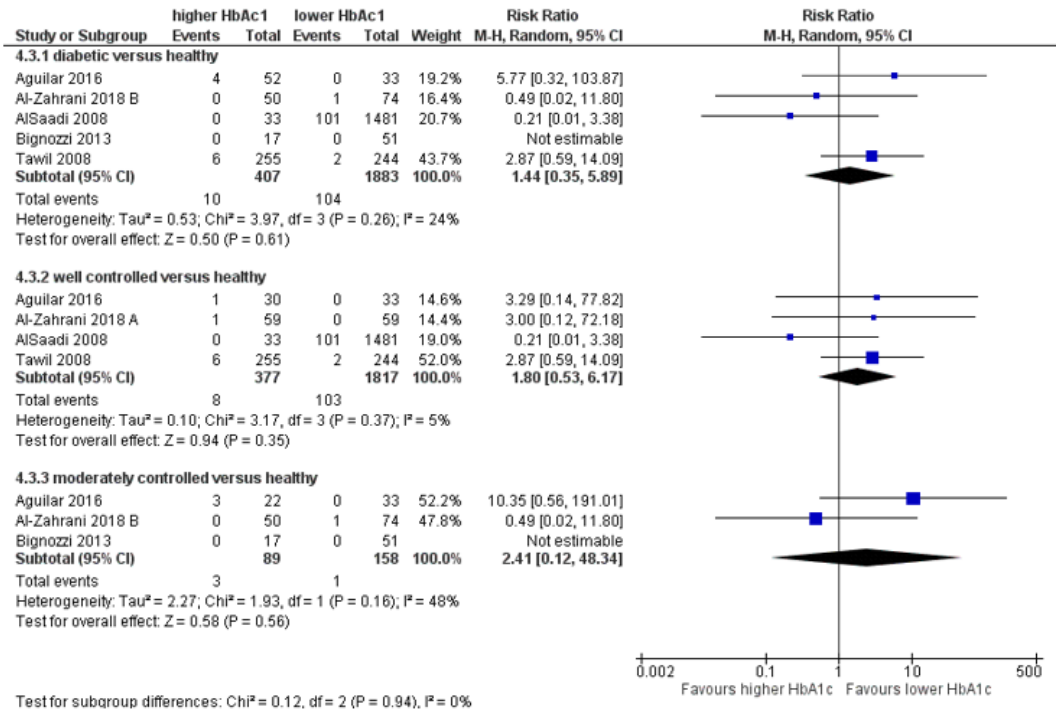

Figure 3: Forest plot of implant loss at 24 months

DISCUSSION

Diabetes mellitus classified into two main types in literature. Type I, insulin dependent diabetes, constitutes 6–10% of total diabetic patients.[46] While, Type II is non-insulin dependent diabetes mellitus and occurs in 90 to 94% of diabetic patients. [47] The role of type II diabetes on the dental implants failure was reported in many studies, On the other hand type I was rarely reported in literature. Even in this SR, all studies included type II diabetes except Alsaadi 2008[31] included both types. The classification of diabetic patients varied in included studies. Some studies[35, 42, 42] classified diabetic patients based on a HbAc1 levels above 6%, while many studies above 6.5 and 7%.In addition to, some used FPGL, while others were self-reported. Therefore, in this SR only studies with definite cut off points were included and studies were only pooled, when the groups of patients were well defined.

Implant failure as described by the criteria of Albrektsson 1986[(49)] was sought for, in 5 studies [41 42, 38, 30 31]. However, its results were reported as implant loss, while neglecting all other criteria of failure. The results of our meta-analysis showed no statistically significant difference regarding implant loss in diabetic and healthy patients. These results are in accordance with a previously published SR; Naujokat et al 2016[12] which was based on a qualitative synthesis rather than a quantitative one and for a follow up period up to 6 years. Similarly, a meta-analysis performed earlier by Charconovic et al [49] revealed no significant difference between healthy and diabetic patients regarding this outcome at RR 1.07[0.8,1.44] P= 0.65. Oates 2009,[24] Oates 2014[35] and Tawil 2008[44] also found no significant difference between healthy and diabetic patients regarding implant loss. On the other hand, 2

retrospective studies [48, 31] and 1 prospective study [34] found a significant difference in implant loss between healthy and diabetic patients, surprisingly favoring diabetic patients.

Besides, duration of diabetes in the included studies is variable. It was found to have a significant impact on the results of implant loss and difference between findings of this SR and other studies might be attributed to a difference in the diabetic duration, in addition to other confounding factors that might affect the results. Olson[50] did a regression analysis and concluded that the duration of diabetes is significantly associated with implant failure ($P<0.025$). The short term hyperglycemia seems to have no detrimental effects on peri-implant health as does hyperglycaemia in chronic decompensated diabetic patients, since insulin not only has an effect on hyperglycaemia, but may also controls and even stimulates osteoblastic activity. [51,52]

Sensitivity of the results of implant loss to the different levels of glycemic control, moderately and well controlled diabetic patients were compared to healthy subjects separately and in conjunction. The results showed no significant impact for the glycemic level on the results of implant loss. This might be attributed to fact that implants in diabetic patients do not undergo implant loss at the studied follow up periods. Instead, signs of implant failure like peri-implant mucosits, peri-implantitis and marginal bone loss seem to be more sensitive to higher glycemic levels.

CONCLUSIONS

Based on the results of implant loss 2 years following implant placement, implant therapy in diabetic patients seems to be possible. However, results should be taken with extreme cautions, since the quality of evidence is very low

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