Impact of diabetes mellitus on dental implants: A cross sectional controlled clinical study

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Background and objective: After osseointegration the long-term success of dental implants is determined by the maintenance of the peri-implant soft tissue and bone level. This study evaluates the impact of Diabetes mellitus on dental implants in diabetic patients and compare it with that of nondiabetic patients.

Patients and methods: Thirty diabetic patients and thirty controlled subjects rehabilitated with dental implants were included in this study. The duration of implant treatment is (1-7) years, and dental implant status between both groups was compared using Immunohistochemistry for analyzing Interleukin 6 in peri-implant crevicular fluid, bacteriology, radiology, and clinically by measuring gingival sulcus depth, bleeding on probing, gingival recession, presence of suppuration and mobility. The statistical package for the social sciences program (SPSS, version 28) was used for data analysis.

Results: Diabetic patients show a Statistically significant difference to non diabetic subjects in the level of interleukin 6 with (P value 0.004), Culture and sensitivity with (P value 0.003), Peri -implant bone loss in mesial and distal sides of the implant with P values 0.006 and 0.002 respectively, and also, in gingival recession with (P value 0.017). while the difference was not significant in gingival sulcus depth P value0.220, bleeding on probing P value0.550, implant suppuration P value 0.999, and mobility P value 0.999.

Key words: Bacteriology, Diabetes mellitus, Interleukin 6, osseointegration, Periimplantitis

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INTRODUCTION

Currently dental implants are the most preferred therapeutic modality for the management of partially and completely edentulous arches. The success of dental implants is determined by several factors: proper patient selection, precise clinical and dental laboratory techniques, occlusal factors, and maintenance of postoperative oral hygiene. [1] Proper case selection arguably the most essential factor for the success of dental implant treatment, depends on choosing patients in whom wound healing and metabolic stability exist. Some conditions transform the normal body response to a surgical insult, but once controlled, fail to amend implant survival . [2] Although dental implants show a high long-term success rate, but certain risk factors can compromise the biological process of osseointegration or adversely affect the maintenance of peri-implant health. Diabetes is among these factors. [3] It can be determined as a relative contraindication for successful dental implant treatment. 2 Diabetes mellitus is the most common endocrine disease, characterized by hyperglycemia as a result of a defect in insulin secretion and/or insulin action. t is a significant global public health burden that contributes to morbidity and mortality. [4] diabetes mellitus has a high prevalence and dramatically increasing. According to predilections the number of diabetic patients will reach 300 million patients worldwide in 2025 at the time it was 135 million in 1995. [5] International Diabetes

Federation discussed that the number of people aged 20 to 79 years with diabetes mellitus had risen to 424.9 million in 2017, roughly three times the prevalence in 2000. And it will reach 629 million by 2045. [6] Increased susceptibility to infection, delayed wound healing, and microvascular complications are from the adverse sequelae of Poorly controlled diabetes mellitus. [5] Diabetes mellitus is an extremely significant disease from the point of view of dental implant therapy. It is well-established that a chronic hyperglycemic state impairs periodontal structure and functions, it could have a direct effect on the health of the periodontium and, consequently, the need for dental implant therapy. Diabetes patients have a persistent inflammatory response, significant attachment loss, and [3] increased alveolar bone resorption. [7] Preservation of the peri-implant soft tissue and bone level determines the long-term stability of dental implants. Nonetheless, after osseointegration, biological complications can induce, and/or increase tissue loss around the implants, thereby adversely affecting the rehabilitation course. [8] Implant placement for diabetic patients was contraindicated as it causes Problems with wound healing or bone metabolism. [9] And Chambrone L, Palma LF, [8] showed that Chronic hyperglycemia is considered a risk factor for peri-implant diseases, and Implant rehabilitation has not historically been proposed for uncontrolled diabetes mellitus patients. Dental implant treatment is not limited to systemically healthy individuals, Diabetes mellitus patients require special attention in dental implant treatment, and Diabetes mellitus patients are potential candidates for dental implant treatment. And fewer complications will face diabetic patients whose disease is well-controlled. [10] When peri-implant tissue is stimulated by bacterial biofilm, the host's inflammatory and immunological response leads to the loss of peri-implant tissue in diabetic and prediabetic patients. [8] hyperglycemia present in diabetic patients leads to excessive formation and accumulation of advanced glycation end-products (AGEs), this reduce the synthesis of matrix proteins (e.g., collagen and osteocalcin) by fibroblasts and thereby leads to structural and functional periodontal damage. [7] The AGEs and the interaction of their corresponding receptors activates the expression of destructive inflammatory cytokines in the serum and gingival fluid, such as (Interleukin-6, Interleukin-1beta, Tumor necrosis factor alpha, IL-6, IL-1b, and TNF -a). This process leads to the exacerbation of inflammation and bone loss around dental implants. [8,11] Till now there is a lack of sufficient data and study about the effect of Diabetes mellitus on the dental Implant status in the Iraqi Kurdistan region. This study evaluates dental implant status in diabetic patients and compares it with that of non-diabetic patients.

Aims of the study: Evaluation of the dental implant status in diabetic versus non-diabetic patients by:

- Measurement of peri-implant bone loss by digital Orthopantomography (OPG).
- Clinical evaluation of implant sites including measurement of gingival sulcus depth, recession, presence of mobility, bleeding on probing and suppuration.
- Evaluation of Peri-implant crevicular fluid (PICF) in patients with Diabetes mellitus by Immunohistochemistry Test and compare it with that of non-diabetic patients.
- Evaluation of bacteriology of diabetic and non-diabetic patients.

METHODS: The study is a Cross-sectional, clinical, hospital-based study. Conducted in dental implant Unit in Oral and Maxillofacial Surgery department / Rizgary teaching hospital in Erbil/ Iraqi Kurdistan region. The study protocol was initially reviewed and then approved by the Ethical Committee of Hawler Medical University. Inclusion criteria: All Patients Diagnosed to have Diabetes mellitus and had dental implant treatment in Rizgary teaching hospital. Exclusion criteria: 1-Patients with any medical condition that affect the Immune system other than Diabetes mellitus, such as acquired immune deficiency syndrome/HIV. 2-Patients that had used medications such as steroids. 3- Smokers and alcohol consumption.

Study participants: Patients were selected after searching for a key word Diabetes mellitus, from 5000 case files of patients

that had dental implant treatment from 2015 -2021 in the dental implant Unit- Oral and Maxillofacial Surgery department /Rizgary teaching hospital. All of the patients were non-smokers, diabetic patients were type 2 and all of them were on antihyperglycemic tablets, only one system of the dental implant was used for them and all Implants which are evaluated were placed by a single operator.

Informed consent: Eligible patients were informed about the purpose and process of the study in the local language (Kurdish) or in Arabic and English, both verbally and in writing. written informed consent was obtained. the patients signed a consent form and they were allowed to withdraw from the research project at any time without any consequences.

Statistical Analysis: Statistical analysis began by entering the data on a computer using a Microsoft Excel worksheet (Excel 2017). The statistical package for social sciences program (SPSS, version 28) was used for data analysis. The numerical variables were checked for normality using Smirnov – Kolmogorov test, then analyzed using a t-test if normally distributed or Mann Whitney U test if not normally distributed. The categorical data were analyzed through Chi-square test or Fisher's exact test if the expected frequency (value) was less than 5 of more than 20% of the cells in the table, p–values ≤ 0.05 were considered as statistically significant.

Evaluation of dental implant status:

1)Peri-implant bone loss: which is defined as the distance from the widest supra crestal part of the implant to the alveolar crest. [7,12] Digital Orthopantomography was used to measure bone loss at mesial and distal side of the implant, which was used by Rakic et al, [13] as well. Peri-implant bone loss was measured on mesial and distal side of the implant, then the calculation of bone loss for both mesial and distal surface was done by dividing the amount of bone loss in mm over the length of the implant multiplied by 100. [14] By that the percentage of bone loss at mesial and distal side was taken for each implant.

2) Evaluation of Soft tissue status around the Implant: as discussed by Lindhe and Meyle (2008), The probing depth, the presence of bleeding on probing and suppuration should be assessed regularly for the diagnosis of peri-implant diseases. [15] **2:1** gingival sulcus depth: gingival sulcus depth was checked on six surfaces of the implant (mesiobuccal/labial, mid buccal, distobuccal/labial, mesio-lingual/palatal, mid lingual/palatal, and distolingual/palatal), then the mean for each implant was derived. [15]

2:2 gingival recession: The recession was checked on six surfaces of the implant (mesio-buccal/labial, mid buccal, distobuccal/labial, mesio-lingual/palatal, mid lingual/palatal, and distolingual/palatal), then the mean for each implant was derived. [15]

2:3 gingival Bleeding Index: also known as (GBI - Ainamo & Bay, 1975) This Gingival Bleeding Index (GBI), introduced by Ainamo & Bay (1975), is performed through the gentle probing of the orifice of the gingival crevice. If bleeding occurred within 10 seconds a positive finding was recorded and the number of positive sites was recorded and then expressed as a percentage of the number of sites examined. [16]

2:4 suppuration: peri-implant suppuration is checked for each implant and if suppuration occurred a positive finding was recorded. [15]

0: No suppuration

1: the presence of suppuration.

2:5 Implant mobility

1- A dental implant can be moved less than 1 mm in the buccolingual or mesiodistal direction.

2- A dental implant can be moved 1 mm or more in the buccolingual or mesiodistal direction, And No vertical mobility.

3- A dental implant can be moved 1 mm or more in the buccolingual or mesiodistal direction, And vertical mobility is present. [17]

2:6 Implant failure: presence of pain, implant disfunction, and implant mobility were determined as factors for implant failure. [17]

3) Laboratory tests: Patients were instructed to rinse their mouths with distilled water. Then the samples were collected for bacteriology and immunochemistry tests from each patient.

3:1 Evaluation of marginal gingival secretion by analyzing interleukin 6: Evaluation was done by immunohistochemistry test. Literally instructions of the manufacturer of enzyme-linked immunosorbent as-

say (ELISA) kit of interleukin 6 was followed. After making the area around sample collection clean, and dry to prevent leakage of the saliva to the site of sample collection, peri implant crevicular fluid was collected by a special collector (Perio paper strip), which was left in place for 30 seconds, the sample is stored inside an (Eppendorf tube 0.5 ml), then 250 micro letters of phosphate buffered saline (PBS) is added. The samples then stored inside (-80-degree) freezer for later analyze of Interleukin 6.

Phosphate buffered saline (PBS) is prepared by adding a packet of powder of the buffer to a letter of distilled water. and the preparation was done in the biochemistry unit/ laboratory department/ Rizgary teaching hospital. Analyzing was done in the laboratory of Soran private hospital.

Results:

1: Immunohistochemistry: Regarding immunohistochemical analysis, diabetic patients showed a statistically highly significant difference in means of interleukin 6. The mean interleukin 6 in diabetic cases was 198.34 pg/ml while in non-diabetic group was 167.67 pg/ml. p-value was 0.004 (Table 1).

3:2 Culture and sensitivity test: a swab was taken from the sulcus of the dental implant. This laboratory test was done in Smart Lab.

Figure 1: Collection of peri implant crevicular fluid for analyzing of Interleukin 6.

Figure 2: An Eppendorf tube (0.5 ml) with the sample and phosphate buffered saline inside it.

Figure 3: taking a sample for Culture and sensitivity test.

Table 1: The difference in mean interleukin 6 between diabetic and non-diabetic groups.

Variable	study group	Mean	S.D	p-value	t-test
interleukin 6	diabetic	198.34	42.45	0.004	Highly significant
	non diabetic	167.67	35.63		

2: Culture and sensitivity test:
Regarding culture and sensitivity tests, the Chi-square test between the two groups showed a statistically highly significant difference in diabetic with a p-value of 0.003. 43.3% of non-diabetic patients got a negative culture test. more than half of diabetic patients 53.3% had streptococcus pyogenes, while only 10% of non-diabetic participants had streptococcus pyogenes Table 2 .

Table 2: Association between study groups in culture and sensitivity test.

Variable	Categories	study group		p-value
		non diabetic	diabetic	
culture and sensitivity test	negative culture	13 (43.3%)	8 (26.7%)	0.003
	streptococcus pyogenes	3 (10%)	16 (53.3%)	
	streptococcus mutans	8 (26.7%)	2 (6.7%)	
	streptococcus oralis	3 (10%)	3 (10%)	
	streptococcus agalactiae	0 (0%)	1 (3.3%)	
	enterococcus faecalis	3 (10%)	0 (0%)	
Total		30	30	
		100%	100%	

3: Clinical evaluation of patients:
Regarding gingival recession, diabetic patients showed a statistically significant difference than nondiabetic patients in the median of gingival recession, Mann – Whitney U test was done and the p-value was 0.017 (Table 3) .

Table 3: The difference of mean gingival recession between diabetic and non-diabetic patients.

Variables	study group	Mean	S.D	Median	p-value	Mann – Whitney U test
gingival recession	diabetic	0.29	0.37	0.16	0.017	Significant
	non diabetic	0.24	0.60	0		

Figure 4: gingival recession in the buccal and mesio-buccal side of dental implant in one of the diabetic patients.

Regarding gingival sulcus depth and gingival bleeding on probing in diabetic and non -diabetic groups, Mann – Whitney U test was used, and diabetic patients had statistically non significant difference than non diabetic subjects in the median of gingival sulcus depth and gingival bleeding with P values were 0.220 and 0.550 respectively table 4.

Table 4: The difference of mean of pocket depth and gingival bleeding in diabetic and non-diabetic groups.

Variables	study group	Mean	S.D	Median	p-value	Mann – Whitney U test
gingival sulcus depth in mm	diabetic	2.69	1.68	2.41	0.220	Non-significant
	non diabetic	2.22	1.16	2		
gingival bleeding in percentage	diabetic	25.54	24.26	16.66	0.550	Non-significant
	non diabetic	21.66	21.50	16.66		

Regarding implant suppuration, there was a statistically non-significant association between study groups and presence of suppuration, the majority (93.3%) of the diabetic group had no suppuration. Fisher's Exact test was done and the p-value was 0.999 (Table 5).

Table 5: Association between study groups and presence of suppuration.

Variable	Categories	study group		P-value
		non diabetic	diabetic	
Presence of suppuration	no	29 (96.7%)	28 (93.3%)	0.999
	yes	1 (3.3%)	2 (6.7%)	
Total		30	30	
		100%	100%	

Regarding implant mobility Fisher's Exact test showed a statistically non significant difference in diabetic patients than non diabetic subjects with a p-value 0.999. (Table 6).

Table 6: Association between diabetic and non diabetic patients in Implant mobility.

Variable	Categories	study group		P-value
		non diabetic	diabetic	
mobility of the dental implant	< 1 mm in buccolingual or mesiodistal direction	29 (96.7%)	28 (93.3%)	0.999
	> 1 mm plus vertical direction mobility	1 (3.3%)	2 (6.7%)	
Total		30	30	
		100%	100%	

Regarding Implant failure rate: the failure rate in diabetic patients was (6.7%). While in non-diabetic patients it was (3.3%) Table 7.

Table 7: Frequency and percentage of suppuration and mobility of dental implants.

Variables	Categories	Frequency	Percent
implant failure in the diabetic group	not failed	28	93.3%
	implant failed	2	6.7%
implant failure in non-diabetic group	not failed	29	96.7%
	implant failed	1	3.3%
Total		30	100

4: Peri-implant bone loss: Regarding peri -implant bone loss, diabetic patients had a statistically highly significant difference than non diabetic patients. In the mesial side of the implant, diabetic patients had a statistically highly significant difference in the median of the percentage of bone loss in mesial side of the implant, diabetic cases had a larger amount 27.91% of bone loss in comparison to non-diabetic group who had 16.66% of bone loss in the mesial side of the implant, Mann – Whitney U test was done and p-value was 0.006 table 8. and regarding bone loss in the distal side of the implant, diabetic patients showed a statistically highly significant difference in the median of percentage of bone loss in the distal side of the implant than non diabetic

subjects, diabetic patients had 29.28% of peri-implant bone loss in reverse to non-diabetic patients who had 16.66% of bone loss in the distal side, Mann – Whitney U test was performed and p-value was highly significant 0.002 more detail in Table 8.

Table 8: Percentage of bone loss in mesial and distal side of the implant in diabetic and nondiabetic groups.

Variables	study group	Mean	S.D	Median	p-value	Mann – Whitney U test
percentage of bone loss in mesial side	diabetic	30.21	15.70	27.91	0.006	Highly significant
	non diabetic	20.68	13.22	16.66		
percentage of bone loss in distal side	diabetic	30.69	17.87	29.28	0.002	Highly significant
	non diabetic	18.78	8.51	16.66		

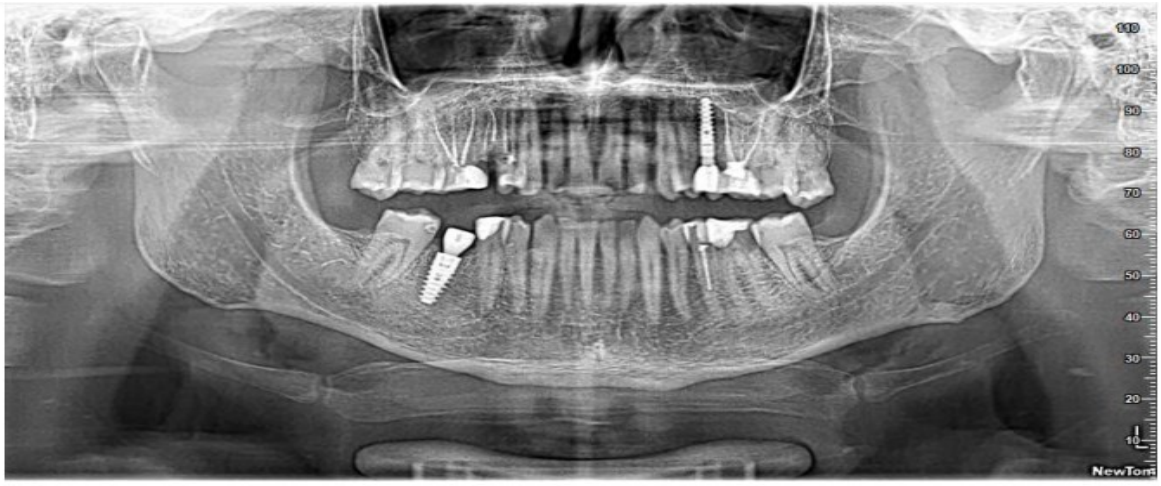

Figure 5: implant placement in lower right first molar.

Figure 6: peri implant bone loss and implant failure in lower right first molar after 3 years of placement.

DISCUSSION

Replacing missing teeth with dental implants is safe and effective, with a high success rate, despite certain factors that can influence the outcomes, including certain effects of diabetes mellitus on the osseointegration process in diabetic patients. [7] This study was designed to evaluate dental implant status between patients with and without diabetes mellitus. The result of this study showed that patients with diabetes mellitus had a significantly higher level of IL6 than non-diabetic patients. this result agreed with studies by Isola et al. [18], He et al. [19], and Radaelli et al. [20], who reported that patients with diabetes usually have salivary IL-6 levels significantly higher than healthy individuals, exposure of the peri-implant area to certain pathogens in diabetes patients might be one of the reasons. While the result of the study by Zhou et al. [21] disagreed with this study, and showed that the level of interleukin 6 is decreased, the sample size might be the reason for the result of this study as they recommend further studies with a larger sample size to validate the finding of their study. On the other hand, diabetic patients showed a statistically significant difference than non-diabetic subjects regarding culture and sensitivity test, with streptococcus specious predomination. streptococcus pyogenes is the most isolated bacteria in the diabetic group, while streptococcus mutans was the most isolated in non diabetic subjects. This result agrees with Yeh et al. [22] which found that Streptococcus spp. are more common to sites with peri-implantitis.while according to Celakovsky et al. [23] and, Fu and Wang [24] the isolated bacteria was different in comparison with this study, the bacteriology was polymicrobial, including both aerobic and anaerobic bacteria, the incidence of anaerobic bacteria was higher. Microbiologic methods used to study the presence of microorganisms in peri-implantitis sites seem to influence results of the microbial profile studies. And Currently, microorganisms are best identified using polymerase chain reaction (PCR). The gingival sulcus depth and bleeding on probing are considered key elements in diagnosing inflammation in the peri-implant mucosa. [25] Patients that pass through dental implant treatment in dental implant unit in Rizgary teaching hospital have regular follow up both clinically and radiographically. Regarding peri-implant gingival sulcus depth, and bleeding on probing this study shows no statistically significant difference between diabetic and non-diabetic patients. Tow studies by Al Amri et al, [26] and Alsahhaf et al, [27] also reported a statistically non significant difference between diabetic patients and 15 patients without diabetes regarding gingival sulcus depth and bleeding on probing. oral hygiene maintenance lowers peri-implant inflammatory parameters especially in type 2 diabetes mellitus. A study by Al Amri et al, [26] showed that type of a dental implant loading has an effect on clinical status of dental implants, as with delayed loading, there was no statistically significant difference in gingival sulcus depth and bleeding on probing between patients with and without diabetes. however, in diabetic patients with immediate loading implants gingival sulcus depth and bleeding on probing were significantly higher. While according to Al Zahrani and Al Mutairi, [7] Lagunov et al, [25] and Jiang et al,[6] gingival sulcus depth and bleeding on probing in diabetic patients are significantly higher than that of non-diabetic patients, bad oral hygiene, life style of patients and uncontrolled level of blood sugar are the reason for the result.

Regarding gingival recession this study showed that diabetic patients has a statistically significant difference than non-diabetic subjects. This result agrees with an earlier studies by Jepsen et al, [28] and Jung et al, [29] Microvascular dysfunction in diabetes mellitus with time causes microvascular disease in any tissue in the body including gingival tissue and leads to tissue loss. [29] while Sanz et al, [30] stated that there is no direct link between diabetes and gingival recession, In an international workshop between the European Federation of Periodontology (EFP) and the International Diabetes Federation (IDF) in 2018, the role of genetic factors in developing gingival recession was highlighted. [31]

Regarding Implant suppuration, implant mobility and failure in diabetic patients were higher than in nondiabetic patients, but the difference was not statistically sig-

nificant. This result agrees with studies by Sghaireen et al, [32] and Andrade et al,[33] who stated that well glycemic control patients do not have a higher degree of implant mobility, suppuration and failure rate in comparison to healthy individuals. While according to a study by Ansari et al, [34] there is a statistically significant higher mobility, suppuration and failure rate in diabetic than non-diabetic patients. Level of blood sugar, type of surface treatment of the implant, location of implant placement, and type of diabetes also plays a role in implant mobility and failure, as patients with type I diabetes are much more likely to lose an implant than patients with type 2 diabetes mellitus.

Regarding peri-implant bone loss, the result showed that patients with diabetes mellitus had a significantly higher level of bone loss than non-diabetic patients. Erdogan et al, [35] and Alsahhaf et al, [27] reported higher marginal bone loss in diabetes patients than that in patients without diabetes, but the difference was not statistically significant. While findings of several earlier studies by (Al Amri et al, [26] Al Zahrani and Al Mutairi, [7] Lagunov et al, [25] Isola et al, [18] Ansari et al, [34]) agreed with this study and showed that bone loss values of diabetes mellitus patients were significantly higher than that of nondiabetic patients. High expression of proinflammatory cytokines has been observed in bone tissue, supporting the idea that the bone itself produces an inflammatory response in diabetes mellitus patients. [25]

Conclusion: Diabetic patients are more susceptible to bone loss than non-diabetic patients, as they have a higher level of proinflammatory cytokine (Interleukin 6) and different bacteriological backgrounds. according to this study streptococcus pyogenes are predominant bacterial pathogens in diabetes mellitus, they are penicillin-resistant, also considered resistant to ampicillin, amoxicillin, amoxicillin / Clavulanic acid, and ceftriaxone. So, for the treatment of periimplantitis in diabetes mellitus other antibiotics could be recommended.

Conflicts of interst

The authors reported no conflicts of intersts

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