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Dental Implants in Diabetic Patients: A Review

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Review Article

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ABSTRACT

Dental implants have currently been recognized as an acceptable treatment modality for the replacement of missing teeth, but diabetes mellitus is considered a relative contraindication for dental implant therapy. As periodontal disease is the sixth major complication of diabetes, these patients are at increased risk for teeth loss. Due to this, these patients may be denied the benefit of dental implants. Hence, the aim of this review is to report findings of various studies wherein implants were placed in diabetic individuals so as to improve the understanding of the possibilities and aid in decision making for implant therapy in patients with diabetes.

Keywords: Dental Implants, Diabetes Mellitus, Glycosylated Hemoglobin.

Introduction

Missing tooth does not produce immediate complications; however, failure to replace missing teeth will eventually lead to various consequences such as tipping of adjacent teeth, supra eruption of opposing teeth, loss of alveolar bone support.

The rehabilitation of partially and fully edentulous patients with implant-supported restorations has become a standardized and predictable therapy resulting in high survival and success rates for both implants and the restoration. As implants are anchored directly into bones, they provide increased stability, giving a more natural appearance. Dental implants also minimize the risk of bone resorption and atrophy, in contrast to other traditional restoration methods. It involves osseointegration and periodontal wound healing.[1]

Dental implants provide the patient with additional benefits previously unavailable for enhancing function and/or aesthetics. Although replacement of teeth with dental implants is an effective treatment modality, their predictability relies on successful osseointegration formed during the healing period.

Osseointegration is defined as a direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant. Long-term maintenance of osseointegration results in the successful prosthetic rehabilitation of both fully and partially edentulous patients.[2]

However, various systemic disorders such as osteoporosis, cardiovascular disorders, etc. adversely affect the osseointegration of dental implants. One such metabolic disorder is type 2 Diabetes Mellitus.[3]

Diabetes mellitus is the most prevalent endocrine disease affecting 5% to 10% of the overall population. Diabetes presents in two forms:
Type 1: Insulin-dependent Diabetes Mellitus
Type 2: Noninsulin-dependent Diabetes Mellitus.

Only about 10% to 20% of all diabetics are insulin-dependent. The remaining 80% to 90% are noninsulin-dependent.

Insulin is an anabolic hormone produced in the pancreas. When insufficient amounts of insulin are present, glucose is not efficiently transported into cells and adipose tissues, and hyperglycemia occurs.[4]

Being a complex syndrome, diabetes is responsible for numerous complications. Type -1 diabetes causes decreased bone mineral density, as well as reduced bone formation and higher bone resorption.

Type -2 diabetes produces normal or greater bone mineral density in some patients. Insulin not only reduces the adverse effect of hyperglycemia by controlling it but also stimulates osteoblastic activity. Hence, bone matrix formation in insulin-treated experimental models is similar to control ones. Type 2 diabetics experience a 2.8 to 3.4 times higher risk of developing periodontitis than non-diabetics. Periodontitis is considered the sixth complication of diabetes.

Diabetic patients seem to be more prone to infection, and that healing after surgery is slower. High circulating levels of glucose inhibit peripheral leukocyte chemotaxis, providing a nutrient-rich environment for bacterial or fungal replication. Because of such considerations, diabetes mellitus remains a relative contraindication for dental implant therapy. Based upon the person's level of glycemic control, many persons with diabetes may be denied the benefits of implant therapy. Hence, this review focuses on reporting findings of various implant studies conducted in diabetic patients so as to improve the understanding of the possibilities for implant therapy in patients with diabetes.[5]

Dental Implants in Diabetic Patients: The placement of dental implants in diabetic patients remains controversial. Defined guidelines with objective criteria including type of diabetes, age of onset, and level of long-term control i.e., glycated hemoglobin level (HbA1c) remain to be established. A clinical judgment is assessing the risk level of an individual patient. A patient with late-onset disease, diet control, tooth loss not associated with periodontitis, and a single-tooth indication may have the lowest risk of implant failure. Conversely, a patient with insulin-dependent juvenile diabetes, tooth loss as a result of periodontal disease, and a total edentulous indication may be at the highest risk of implant loss.[6]

Kapur KK et al.[7] (1998) conducted a study in which he divided 89 patients treated with or without insulin into 2 groups, 37 patients received conventional, and 52 received implant-supported dentures. HbA1c levels <13.0% were included in the study. Treatment was successful in 56.9% of patients with conventional dentures

and 72.1% with overdentures. Significant improvements have been observed with both the treatment modalities. They concluded that in the absence of any undue complications, implants can be successfully used to support dentures in diabetic patients even with low to moderate levels of metabolic control.

Thomas J. Balshi et al.[8] (1999) in a study reported the results of implants in 34 patients with type 2 diabetes who were treated with 227 dental implants. At the second-stage surgery, 214 of the implants had osseointegrated, a survival rate of 94.3% was reported. Only one implant among the 177 implants failed, which were followed through final restoration, with a clinical survival rate of 99.9%. He concluded that to increase the chances of successful osseointegration, screening for diabetes, and trying to ensure that implant candidates are in metabolic control are recommended.

Olson et al.[9] (2000) assessed the success of 178 implants placed in the mandibular symphysis region of 89 patients with well-controlled type 2 diabetes over a period of 5 years. 16(9.0%) of the178 implants failed. They observed that only duration of diabetes and implant length be statistically significant predictors of implant failure after analyzing the outcomes against variables such as baseline and follow-up fasting plasma glucose, baseline and follow-up HbA1c values, subject age, duration of diabetes, baseline diabetic therapy, smoking history, and implant length. They concluded that the duration of diabetes may be associated with implant failure and that longer implants experience fewer failures.

Peled M et al.[10] (2003) conducted a study on 41 patients who received 141 implants for retention of overdentures. They reported a success rate of 97.3% and 94.4% at the end of 1 and 5 years, respectively, following implantation. Improvement of function has been reported by the majority of patients following the treatment. No significant correlation was found between failed implants and glucose level. They concluded that the clinical outcomes of dental implants in patients with well-controlled type 2 diabetes mellitus are satisfying and encouraging.

Dowell S et al.[11] (2007) conducted a study to evaluate the relationship between glycemic control and implant success in patients with type 2 diabetes mellitus. A total of 50 non-submerged, non-restored implants were placed in 35 subjects (HbA1c levels 4.5 -13.8%). Outcomes assessed were implant success or failure, clinical complications, and adverse events. They concluded that the glycemic control levels did not influence the clinical success or significant early healing complications associated with implant therapy in subjects with type 2 diabetes mellitus.

Turkyilmaz I[12] (2010) conducted a study to present clinical outcomes of 23 implants placed in 10 patients with well, or moderately well, controlled type 2 diabetes mellitus patients, over a period of 1 year. No bleeding on probing, no periapical radiolucency, or pathologic probing depth was recorded at recall visits. All implants were considered successful at the 1-year follow-up. He concluded that because no evidence of diminished clinical success and/or significant complications related to implant treatment were observed for this patient population, dental implant treatment can be offered to patients with well or moderately controlled type 2 diabetes mellitus.

Khandelwal N et al.[13] (2011) conducted a study to evaluate the potential of a chemically modified Sandblasted, Large grit, Acid-etched (SLA) surface, compared with a conventional SLA surface. Forty-eight implants were placed in 24 poorly controlled type 2 diabetic patients (HbA1c levels 7.5–11.4%), with a minimum of two posterior mandibular tooth sites. Implant stability (ISQ) was assessed at baseline, 2, 3, 4, 6, 8, 10, 12, and 16 weeks following implant placement. Forty-seven (98%) of the 48 implants were successfully

osseointegrated. They concluded that implant stabilization was similar for the chemically modified SLA implants and the conventional SLA implants in type 2 diabetic patients presenting with poor glycemic control. This study also demonstrated clinically successful implant placement even in poorly controlled diabetic patients.

Tatarakis N et al.[14] (2014) conducted a study in 32 subjects, having at least one functional implant and six teeth, and were divided into groups (1) type 2 diabetes mellitus and (2) non-diabetic controls, for a 1-year longitudinal investigation. None of the parameters have shown a significant difference among the two groups except for a significant increase in the probing depth of implants in the diabetes group from baseline to 1 year. They concluded that the clinical, microbiological, salivary biomarkers of dental implant patients with type 2 diabetes who are under regular maintenance care and good metabolic control were very similar to those of non-diabetic individuals.

Oates Jr TW et al.[15] (2014) conducted a study to determine whether type 2 diabetic patients with poor glycemic control are contraindicated for dental implant therapy. A total of 234 implants were placed in 117 patients. Implant survival and stability were assessed relative to baseline glycated hemoglobin A1c (HbA1c) levels up to 11.1 % and as high as 13.3 % over a period of one year. Implant survival rates were 99 % for patients who did not have diabetes; 98.9 % for those with well-controlled diabetes and 100 % for those with poorly controlled diabetes. They concluded that alterations in early bone healing and implant stability were associated with hyperglycemia. However, elevated HbA1c levels were not associated with altered implant survival one year after loading.

Erdogan Ö et al.[16] (2015) evaluated the clinical outcomes of dental implant therapy in type 2 diabetic patients. Forty-three implants were placed in 24 patients: (1) 22 implants in patients with diabetes, and (2) 21 implants in patients without diabetes, using staged guided bone regeneration procedures, over a period of 12 months. The edentulous maxillary anterior/premolar regions with inadequate horizontal width but sufficient vertical height were treated with a staged guided bone regeneration technique. The survival rate was 100% for both groups. In group 1, the success rate was 95%, and in group 2, the success rate was 100 %. None of the parameters have shown a significant difference between the two groups. They concluded that well-controlled type 2 diabetic patients (HbA1c levels below 7.5 %), requiring dental implants can undergo staged GBR procedures securely.

Aguilar-Salvatierra A et al.[17] (2015) conducted a study to evaluate implant survival and primary stability parameters in patients with diabetes with different levels of glycosylated hemoglobin A1c (HbA1c). They divided 85 patients into three groups according to their HbA1c levels: (1) 33 patients (<6, control group); (2) 30 patients (6.1–8); and (3) 22 patients (8.1–10) who were treated with immediate placement of implant-supported, single-tooth replacements over a period of 2 years. The implant survival rate was analyzed among all the groups, with three variables to evaluate the peri-implant health: probing depth, bleeding on probing, marginal bone loss. They concluded that patients with diabetes can receive implant-based treatments with immediate loading safely, providing they present moderate HbA1c values.

Ghiraldini B et al.,[18] (2015) conducted a study on type 2 diabetes mellitus (T2DM) patients to determine whether glycemic control influences the stabilization of implants and the levels of bone markers in peri-implant fluid during healing, over a period of 12 months. Patients indicated for implant therapy were recruited into three groups (1) systemically healthy patients (2) better-controlled T2DM (HbA1c levels ≤ 8%); and (3) poorly controlled T2DM (HbA1c levels > 8%.). The implant stability quotient (ISQ) was determined, the peri-

implant fluid levels of fibroblast growth factor (FGF), transforming growth factor- β (TGF-β), osteocalcin (OC), osteopontin (OPN), and osteoprotegerin (OPG) were quantified at 15 days, and 3, 6, and 12 months. They concluded that poor glycemic control negatively modulated the bone factors during healing, although T2DM, had no effect on implant stabilization regardless of glycemic status.

Eskow CC, Oates TW[19] (2017) conducted a study to evaluate survival and clinical complications of 72 dental implants placed in 24 types 2 diabetic individuals with poor glycemic control (HbA1c levels 8-12%). Survival was evaluated after one year and two years. Clinical complications were evaluated in 18 participants after 21-34 months. Survival rates were 98.6% after one year and 96.6% after two years. Complications like peri-implant mucositis were identified in 29% of the participants. No correlation was found between HbA1c level and the occurrence of complications or mucositis. They concluded that dental implants can be safely placed in type 2 diabetic individuals with poor glycemic control, high survival rates, and limited complications.

Ormianer Z, Block J, Matalon S, Kohen J[20] (2018) in a retrospective study evaluated the cumulative success rate of 1112 dental implants placed in 169 patients, using three different insertion protocols: (1) implants immediately inserted following tooth extraction; (2) implants inserted 6 to 8 weeks after tooth extraction to allow for primary healing; (3) implants inserted 4-6 months after tooth extraction, who presented with moderately controlled diabetes (HbA1c ≤ 7-8%), over a period of 8.7 years. The overall success rate was 94%. They concluded that comparable to data published earlier, no statistical significance in survival rate was found between the diabetic and non-diabetic population. The delayed insertion protocol presented with less bone loss compared with other insertion methods.

Glycosylated Hemoglobin Assay: Over the years, type 2 diabetes has been considered a relative contraindication for dental implant therapy. It is certain that dental implants are usually contraindicated in poorly controlled diabetic patients. Evidence from the literature suggests that patients with controlled diabetes have similar success rates for dental implants as healthy individuals. This is further demonstrated, as implant failure rates were found to correlate with the duration of disease but not with levels of hemoglobin A1C (Glycosylated hemoglobin) For patients already diagnosed with diabetes, the hemoglobin A1c test (HbA1c) is used to monitor the patient's overall glycemic control. Glycohemoglobin is formed continuously in erythrocytes as the product of a process called glycosylation, a nonenzymatic reaction of the amino (N)-terminal valine residue of hemoglobin A. The binding of glucose to hemoglobin is highly stable; therefore, hemoglobin remains glycated for the life span of the erythrocyte, i.e.120 days. Therefore, HbA1c is used to measure glycemic control over the previous 3 months.[21]

Before planning for implant surgery, Glycosylated Hemoglobin Assay, or HbA1c should be evaluated. This assay provides the clinician with the average glucose level over the 2-3 months preceding the test. HbA1c value less than 6% is considered normal. Previously, Glycosylated Hemoglabin Assay was not considered a diagnostic test as it does not account for short-term fluctuations in plasma glucose levels. According to the revised criteria by the American Diabetes Association 2018, HbA1c ≥ 6.5% is considered as one of the criteria for a diagnosis of type 2 diabetes.

Evidence from the literature suggests that improved glycemic control is associated with reduced risk of long-term diabetic complications of diabetes such as nephropathy, neuropathy, and retinopathy. Diet control, exercise, and medications are thought to play a major role in the management of glycemic control. In recent times, patients are educated and counselled to bring their glucose levels close to normal, whenever possible. There is some evidence that the risk and severity of periodontal diseases decrease with optimal glycemic

control. Very few studies have examined the levels of glycated hemoglobin in diabetic patients undergoing implant therapy.[22]

Hyperglycemia may adversely affect the clinical outcomes of implant therapy, and glycemic control is considered crucial for determining the success of implants in individuals with type 2 diabetes. Patients with poor glycemic control may present an elevated risk of post-operative complications, such as infection and delayed wound healing.[23]

Possible Risk Factors for the Diabetic Implant Patient[24]

- Type of diabetes
- Age of onset
- Elevated blood glucose levels
- Regiment of glycemic control
- Increased HgA1c levels
- History of tooth loss due to periodontitis
- Poor or insufficient wound-healing history
- Extent of edentulism
- Smoking

Possible Diabetic Disturbances in the Implant Wound-Healing Process:[10]

Surgical Implant Osteotomy	
Blood clot formation	Changes in wound healing proteins
Bone resorption phase	Decreased number of osteoclasts
Matrix formation phase	Inhibition of collagen formation
Bone deposition/ Osteoid mineralization	Decreased number of osteoblasts Mineralization proteins reducted
Maintenance of Osseointegration	Reduced bone turnover Alteration in bone homeostasis Change in diabetic status

Effects of Diabetes on Bone Formation: The impact of diabetes on systemic health has resulted in numerous investigations at the clinical and pre-clinical level. As the effects of diabetic complications are recognized, researchers are examining pathogenesis. It is well known that diabetes-specific complications are related to long-term increases in blood glucose concentrations.[25]

At the molecular level, there are both reversible and irreversible interactions with glucose metabolites. Reversible interactions occur as glucose metabolites react with proteins to form Schiff bases which then transform to Amadori-type early glycosylation products. The amount of early glycosylation products is positively correlated to increases in glucose. A recognized early glycosylation diagnostic product, hemoglobin A1c, is utilized to detect recent levels of glycemic control in monitored patients. It typically defines blood glucose levels over the previous 90 days. Irreversible advanced glycosylation end-products form as a result of a series of chemical rearrangements of the Amadori product and reactions with other molecules. These advanced glycosylation endproducts accumulate over a period of years on long-lived macromolecules such as proteins and lipids. This build-up is a function of glucose concentration and time. However, small changes in glycemic control can affect the number of advanced glycosylation end-products, since formation is by second-order kinetics as a function of glucose concentration. Advanced glycosylation end-products further produce free radicals, which may then react with complexes that are already present.[26]

Qualitative and quantitative changes in extracellular matrix components such as collagens, laminin and vitronectin are caused by advanced glycosylation end-products. These changes induced by advanced glycosylation end-products affect cell adhesion, growth, and matrix accumulation. Additionally, hyperglycemic states may alter DNA and nuclear proteins, since these are also targets of advanced glycosylation end-products.[27]

There are specific alterations in bone metabolism associated with diabetes. Insulin not only is an important hormone for glucose control but has a role in modulating normal skeletal growth. Insulin does not regulate bone resorption but stimulates bone matrix synthesis. Insulin effects are both direct and indirect on bone metabolism. Directly it stimulates osteoblastic matrix synthesis and indirectly it stimulates insulin-like growth factor-I production by the liver. Insulin-like growth factor-I then increases matrix synthesis by two mechanisms: by increasing the number of osteoblasts present and by upregulating the function of differentiated osteoblasts.

Additional bone characteristics including mineral homeostasis, osteoid production, and bone formation are also reduced in experimental diabetic models. Goodman & Hori reported that the amount of mineralized bone and volume of the bone matrix is reduced in these animals. In addition, the lag time for osteoid mineralization is increased for the uncontrolled group.[28]

Bone turnover is decreased as measured by the percentage of osteoclasts, osteoblasts, osteoid surface present, failure to uptake tetracycline labeling, and decreases in osteocalcin synthesis. Lastly in the same study, diabetic animals treated with insulin demonstrate bone growth and osteoid formation at rates similar to controls.[29]

Precautions to Be Taken in Diabetic Patients While Planning for Dental Implant Therapy:[30]

- Complete health history should be obtained from every individual for implant therapy. If the patient presents with a history of diabetes, additional information about his or her current treatment should be obtained.
- If the metabolic control of diabetic patients appears to be inadequate, implant therapy is maybe delayed until optimal control is achieved. High plasma glucose levels have a negative influence on healing as well as the bone remodelling process. In order to ensure successful osseointegration of the implants, and to avoid delay in the healing of gingival tissues, it is essential to maintain good glycemic control before and after surgery. HbA1c value less than 7% is considered a good level of glycemic control.
- The importance of maintaining an acceptable level of metabolic control should be informed to the patient throughout the healing period and taking all diabetic medications on the days of surgery.
- A course of broad-spectrum antibiotics should be started on the day of surgery to reduce the risk of post-operative infection. Amoxicillin (2 gr per os 1 hour previously) is the antibiotic of choice. 0.12% chlorhexidine mouthwash can be prescribed, in addition to antibiotic prophylaxis.
- When multiple adjoining implants were placed, diabetic patients are more prone to implant failures when compared to non-diabetics. As the wound is much larger, the more the number of implants placed adjacent to each other, the more likely they will fail.
- The deleterious effects of smoking on osseointegration has been well documented. The combined effect of smoking and diabetes may substantially increase the risk of implant failure. For this reason,

diabetic patients who have the habit of smoking should be urged to enter a smoking cessation program before planning for implant surgery.

Conclusion: Successful dental implant osseointegration and high implant survival rates can be accomplished in subjects with diabetes with good metabolic control (serum glycemic level and HbA1c in the normal range) in a similar manner as subjects without diabetes. The use of antiseptic mouthrinses and oral hygiene maintenance helps in achieving successful dental implant osseointegration in subjects with diabetes.

Thus, control and treatment of periodontal infections should be an important part of the overall management of patients with diabetes mellitus and consequently could play an important role in successful implant therapy. However, dental implant therapy remains contraindicated in subjects with diabetes without good metabolic control, which is frequently associated with obesity and cardiovascular disease, because of the negative effects of hyperglycemia associated with microangiovasculopathia and AGE accumulation on peri-implant hard and soft tissues.

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