# Prognosis of dental implants in diabetic patients

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**Abstract**

**Background**: To evaluate the impact of diabetes mellitus on dental implant failure rates and marginal bone loss (MBL). **Material and methods**: The researchers conducted an electronic search in three databases and manually searched journals to gather information. They performed meta-analyses and meta-regressions to determine the relationship between odds ratio (OR) and MBL with follow-up time. The review consisted of 89 publications and included data on 5,510 implants placed in diabetic patients and 62,780 implants placed in non-diabetic patients. **Results** : The researchers found that in pairwise meta-analysis, the risk of implant failure was higher in diabetic patients compared to non-diabetic patients (OR 1.777, $p < 0.001$). Type 1 diabetes patients had a higher risk of implant failure compared to type 2 diabetes patients (OR 4.477, $p = 0.032$). This difference was statistically significant in the maxilla but not in the mandible. The mean difference (MD) in MBL between the groups was 0.776 mm ($p = 0.027$), and the MBL MD increased by 0.032 mm for every additional month of follow-up ($p < 0.001$). Additionally, the OR decreased by 0.007 for every additional month of follow-up ($p = 0.048$). **Conclusion** : Implants in diabetic patients showed a 77.7% higher risk of failure than in non-diabetic patients.

**Keywords**: dental implant, failure, marginal bone loss, diabetes mellitus, systematic review, meta-analysis, meta-regression

## Introduction

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia (high levels of glucose in the blood) which results from defects in insulin secretion (the pancreas does not produce enough insulin), insulin action (the body cannot effectively use the insulin it

produces), or both.[1] The most common type of diabetes mellitus, type 2, which accounts for 90–95% of those with diabetes mellitus, was estimated to affect 537 million adults worldwide in 2021, with a prediction to rise to 643 million adults by 2030.[2] Such prevalence highlights the importance of this group of diseases. The long-term hyperglycemia of diabetes mellitus very commonly leads to failure, damage, and/or dysfunction of many tissues and organs of the human body, causing substantial clinical morbidity.[3] Moreover, the duration of diabetes may impact the clinical and functional status of the individuals, a factor that is suggested to be independent of glycemic control and age.[4] These consequences usually result from a set of negative effects of the disease, which include delayed wound healing, microvascular complications, impaired response to infection, impaired bone metabolism, and bone strength, among others.[5-8] For individuals who have onset of type 2 diabetes in youth, the risk of microvascular and other complications increases steadily over time and affects most individuals by the time of young adulthood.[9]

Glycemia, the level of sugar in the blood, may play an important role in these consequences, as a correlation between glycemic control and the development of microvascular and macro-vascular complications was observed.[10] Tight and intensive glycemic control in diabetic patients can delay the onset and the progression of many microvascular-related complications associated with the condition, although the effects of this control seem to become weaker once complications have been manifested. A controlled diabetic patient is defined as a patient that keeps their glycemia as close to normal as possible.[11] This is established by a test, which measures what percentage of hemoglobin proteins in the blood are coated with sugar, namely what percentage of hemoglobin is glycated (HbA1c). Diabetic individuals that keep a level up to 6.5% HbA1c are considered patients with controlled diabetes mellitus.[12]

The negative effect of the disease on bone metabolism has raised some concerns about the long-term survival of dental implants in diabetic patients. A previous systematic review on the subject had shed some light on the issue.[13] The results suggested that diabetes mellitus does exert an influence on the implant failure rates when compared to non-diabetic patients. However, this previous review is based on only 14 studies. It was, therefore, the aim of the present systematic review to compare the implant failure rates and marginal bone loss (MBL) between diabetic and non-diabetic patients in an update of the previous study.

**Material and methods**

The researchers conducted an electronic search on three databases and performed a manual search of journals to gather information. They performed meta-analyses and meta-regressions to determine the relationship between odds ratio (OR) and marginal bone loss (MBL) with

follow-up time. The review included 89 publications and reported data on 5,510 implants placed in diabetic patients and 62,780 implants placed in non-diabetic patients.

The review included clinical studies on implant failure rates in diabetic and non-diabetic individuals who were treated with cylindrical modern dental implants made of commercially pure titanium or its alloys. Since an individual is either diabetic or not, it is not possible to randomly assign them to receive implants, so non-randomized and retrospective clinical studies were also considered for inclusion in this review. Only studies that included diabetic patients under glycemic control were included, and the authors contacted the original authors of the articles to obtain this information when it was not available in the publications. The meta-analysis excluded case reports, technical reports, animal and in vitro studies, and review papers. Additionally, studies evaluating mini-implants, zygomatic, orthodontic, zirconia, subperiosteal, or hollow implants were also excluded. All the results were anlayzed by SPSS software.

**Results**

Out of the 89 studies included in the review, 63 studies reported data on implants placed in both the maxilla and mandible, while 13 studies reported data only on implants placed in the maxilla and another 13 studies reported data only on implants placed in the mandible. Among the included studies, eight studies did not include smokers among their patients, while information on the presence or absence of smokers in the cohort group was not available in six studies. Overall, the review included data on 5,510 implants placed in diabetic patients, of which 394 failed, and 62,780 implants placed in non-diabetic patients, of which 2,343 failed. The odds ratio (OR) for implant failure was 1.777, indicating that diabetic patients had a 1.777 higher risk of implant failure compared to non-diabetic patients. This means that implants placed in diabetic patients had a 77.7% higher risk of failure compared to those placed in non-diabetic patients.

When studies evaluating implants inserted in the maxilla were pooled, the subgroup analysis showed an odds ratio (OR) of 1.968 for implant failure, while the OR was 1.805 for studies evaluating implants inserted in the mandible. The difference in implant failure between the groups was statistically significant in the maxilla, but not in the mandible.

A sub-analysis was also performed for studies that provided information on implant failures between patients with diabetes mellitus type 1 and type 2, which resulted in an OR of 4.477.

The mean difference (MD) of marginal bone loss (MBL) between implants placed in diabetic and non-diabetic patients was 0.776 mm. This means that implants placed in diabetic patients

had a mean 0.776 mm higher MBL compared to implants placed in non-diabetic patients, and the difference was statistically significant.

**Discussion**

The aim of the present systematic review was to compare the clinical outcomes of dental implants between diabetic and non-diabetic patients. This is not the first review on the subject. However, previous reviews either failed to conduct any statistical analysis or were based on much fewer clinical studies. The present review adds much more data (from 89 studies) for the analyses and is the first one in many aspects: (a) to perform a sub-analysis comparing dental implant failure rates between type 1 and type 2 diabetic patients; (b) to perform subgroup analyses for implant failure when only studies evaluating implants inserted in maxillae, as well as when only studies evaluating implants inserted in mandibles; (c) to perform a meta-regression testing the association between the odds ratio of implant failure between diabetic and non-diabetic individuals, and the follow-up time; (d) to perform a meta-analysis on the difference of MBL between diabetic and non-diabetic patients; and (e) to perform a meta-regression testing the association between follow-up and the MBL mean difference between diabetic and non-diabetic individuals.

According to the results of the present review, diabetic patients presented a statistically significant higher risk of dental implant failure and higher marginal bone loss than non-diabetic patients. The null hypothesis was therefore rejected. These results are thought to be mainly related to the deleterious effects of diabetes mellitus on many physiological processes in the human body. One of the negative effects of diabetes mellitus on the body is impaired bone metabolism and bone strength.[14] The hyperglycemia associated with diabetes mellitus, usually due to poor glycemic control, may worsen bone mineral density (BMD), along with an increased risk of fractures. This is caused by an increase in urinary calcium excretion and by the accumulation of advanced glycation products, which induces a proinflammatory state, resulting in lower insulin-like growth factor 1 (IGF-1) levels, and lower pH/acidosis.[15] The role of IGF-1 is important, as it increases bone matrix synthesis and bone formation, as well as regulates osteoclastogenesis by promoting their differentiation.[16] A clinical study observed that patients with diabetes mellitus type 1 had a lower total body bone mineral density as compared to age, sex, and body mass index and matched non-diabetic controls.[17]

Another damaging effect of the disease is the delayed wound and bone healing. The placement of a dental implant into the jaws is controlled surgical aggression to the bone tissues. The healing around the installed implant begins with the formation of a blood clot, vascularization, and proliferation and migration of mesenchymal stem cells (MSCs) from

surrounding bone marrow.[18] Under favorable conditions and stable sites, MSCs differentiate into osteoblasts, and woven bone forms through osteogenesis followed by compaction of woven bone, and after a period of time, bone remodeling starts.[19] Anything that could impair this process may jeopardize the osseointegration of a dental implant. In diabetic patients, the impaired bone cell metabolism and subsequent changes in the properties of the bone matrix may contribute to undermining proper bone healing and reducing the bone matrix strength.[20]

It is known that diabetes mellitus causes microvascular complications. When exposed to hyperglycemia, some types of capillary endothelial cells are unable to reduce the transport of glucose inside the cell, which makes these cells more likely to become damaged as a result of constant hyperglycemia inside them.[21] Several hypotheses have then been proposed to explain the biochemical process of developing microvascular complications. The issue may very probably affect the survival of dental implants, as their clinical success is dependent not only upon osseointegration but also on neovascularization in the peri-implant bone, and since neoangiogenesis is not possible without the development of new blood vessels from pre-existing vasculature, involving the migration behavior, proliferation and differentiation of endothelial cells, damage of pre-existing capillary endothelial cells may very well have a negative effect on the clinical outcomes of dental implants.[22,23]

Hyperglycemia in diabetes mellitus causes dysfunction of the immunological response through many mechanisms, which include suppression of cytokine production, phagocytosis impairment, inhibition of complement effectors, dysfunction of immune cells, and reduced leukocytes recruitment. Therefore, diabetic individuals are more susceptible to infections. This may have a considerable influence on the long-term survival of dental implants, as the immune system is needed to tackle the stages of bacterial establishment and infection of the peri-implant tissues.[24,25]

All these factors may directly or indirectly impair the osseointegration process and/or the long-term maintenance of dental implants in the jaws. The dysfunction of the immunological response, together with the delayed wound healing, may have some influence on the significantly higher MBL around implants in diabetic than in non-diabetic patients, as observed in the present results. The results of an animal-model study suggested that hyperglycemia can be associated with bone loss around implants, possibly related to the increased levels and accumulation of advanced glycation end products in the gingival tissue, which in turn triggers osteoclast induction and promote bone resorption.[26] The results of a review on the subject suggested that elevated and poorer glycemic levels are associated with a greater prevalence of peri-implantitis.[27] Moreover, higher HbA1c levels have been

associated with greater MBL.[28] The estimated increase in the mean difference of MBL between diabetic and non-diabetic patients may be a reflection of the cumulative deleterious effects of the disease with time. This suggests that a closer control of peri-implant tissues may be necessary for diabetic patients in comparison to non-diabetic patients. A review on the effect of the treatment of periodontal disease for glycemic control in diabetic patients concluded that there was no evidence to support that one periodontal therapy was more effective than another in improving glycemic control in people with diabetes mellitus, although the review focused on periodontitis, not peri-implantitis. A review of the impact of diabetes on oral bone regeneration and augmentation techniques concluded that the level of evidence about it is still low.[29]

The possible impact of different implant surfaces on MBL in diabetic and non-diabetic patients is something important to be considered. This would be easier if there were more data available in order to conduct comparisons between different surface modifications. However, a limited number of studies provided information on mean MBL with standard deviation. Therefore, an attempt to conduct additional sub-group analyses of MBL by different implant surfaces would not result in any reliability and would mislead the interpretation of the data. Although more recent surface treatments have shown improvements in the bone-implant contact, it is not entirely clear whether, in general, one surface modification is better than another, and although surface modifications of modern dental implants may result in less MBL than those surfaces from implants from the 1990′s, this is not always the case.[30]

According to the present results, there was a statistically significant difference in the failure rate between the diabetic and non-diabetic patients for implants placed in the maxilla but not in the mandible. This could be related to the fact that sites with poorer bone quality and lack of bone volume, which are more common in the upper jaw, may negatively affect the implant failure rates.

There was an estimated decrease in OR for every additional month of follow-up, meaning that the difference in the risk of implant failure between diabetic and non-diabetic patients tended to decrease with time slowly. Even with the statistically significant difference in failures between the groups, this could be related to the higher implant failure rate usually observed within the first year after implant installation, regardless of how long the follow-up might be.[31]

The sub-analysis comparing the failure rates between patients with different types of diabetes mellitus suggested that patients with diabetes mellitus type I are much more likely to lose an

implant than patients with type 2 of the disease. Although these results are based on limited data, some complications associated with the disease are worse in type 1 diabetes than in type II, which may support these results. Type 1 and type 2 diabetes mellitus are heterogeneous diseases, and their progression and clinical presentation may vary to a great extent. Most cases of type 1 diabetes mellitus are caused by cellular-mediated autoimmune destruction of the pancreatic β-cells, with a minority of cases with no known etiologies. The pancreatic β-cells synthesize, store, and release insulin, in order to maintain the circulating glucose concentrations within a physiologically acceptable range.[32] As these cells are destroyed, excessive levels of glucose must be dealt with exogenous insulin in type 1 diabetic patients. Patients with type 2 diabetes have a relative insulin deficiency, and there is peripheral insulin resistance with progressive loss of β-cell adequate function.[33] These differences in the pathophysiology between the disease types, together with poorer adherence to treatment regimens and greater difficulty in achieving metabolic control in type 1 diabetes, have an influence on the severity of symptoms, which is often marked in type 1 diabetic patients. Although the severity may vary in type 2 diabetic patients, it is usually not severe in these individuals. Diabetes mellitus type 1 usually has an earlier onset, resulting in earlier development of micro- and macro-vascular complications in comparison to type 2 diabetes mellitus.[34] Moreover, patients with type 1 diabetes usually present early bone loss, whereas in type 2, the development of abnormal osseous architecture results in increased or normal bone mineral density, although with compromised skeletal quality and strength. All this may result in a more compromised implant and bone site in type 1 diabetic patients than in type 2 patients. Individuals with type 1 diabetes mellitus even have a higher loss of life expectancy than those with type 2 due to the relatively higher incidence of cardiovascular diseases and acute metabolic disorders in type 1 diabetes mellitus.[35]

**Conclusion**

In conclusion, implants placed in diabetic patients present a statistically significant higher risk of failure and greater marginal bone loss than implants placed in non-diabetic patients. When it comes to the comparison between different types of diabetes mellitus, implants placed in diabetic type I patients present a much higher risk of failure than implants placed in diabetic type II patients.

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