



# Does Vitamin D Supplements are Useful for Osseointegration Dental Implants in Patients with Type 2 Diabetes. Literary Review

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## Abstract

**Background:** Conduct a literature review to determine the relationship between the level of vitamin D in the blood plasma and the osseointegration of dental implants installed in patients with type 2 diabetes mellitus.

**Methods:** In Google Scholar, Medline, Scopus, Web of Sciences, PubMed a systematic review was conducted. Search keywords terms included the relationship between serum vitamin D levels and osseointegration, in relation to vitamin D deficiency and dental implant failure in patients with type II diabetes, the use of vitamin D supplements to enhance osseointegration in patients with type II diabetes.

**Result:** A review of studies showed a significant association between low serum vitamin D levels and osseointegration of dental implants in experimental animals, and a positive effect of vitamin D supplementation on osseointegration were determined.

**Conclusion:** A long-term, multicenter clinical independent study in numerous patients with type II diabetes with implants is needed to examine the relationship between serum vitamin D levels and osseointegration.

## Introduction

The use of dental implants for prosthetics in patients with various forms of toothlessness is currently a widely used procedure, however, osseointegration disorders and peri-implantitis are noted in the literature, especially in high-risk patients [1-4].

The reasons for implant disintegration include many factors, the use of implants in patients with general somatic contraindications, the presence of aggressive periodontitis in the patient, residual inflammatory foci in the implantation area, osteoporosis, contamination of the implant surface, violation of surgical standards, overheating of bones during preparation, damage to

anatomical structures, hypercompression, lack of primary stabilization, premature loading in the presence of contraindications [5-8].

Some of these factors may be more important in patients with insufficient bone tissue and endocrine disorders, including diabetes mellitus and disorders of bone metabolism [9-12].

In recent years, the problem of diabetes mellitus has become particularly relevant due to the widespread prevalence of the disease and the severity of complications among the world's population [13-15].



In diabetes mellitus, damage to various organs and systems is observed, which has many manifestations in the oral cavity [16,17].

According to a number of authors, patients with diabetes often experience gingivitis, stomatitis, caries, the risk of developing periodontitis increases, the function of the salivary glands is impaired, and taste disorders occur. Due to this, the availability of dental services for this group of patients is high and tends to increase [18-20].

As a result of hyperglycemia, patients become susceptible to infections and subsequent complications [21,22].

It should be noted that patients with diabetes also have a high frequency of tooth loss due to the high prevalence of periodontal disease. In this group of patients, the loss of teeth leads to disorders of the digestive system, which can also have a negative impact on the general somatic status of the patient, therefore it is very important to provide them with rational prosthetics in an effective and optimal mode [23].

In patients with diabetes, the effectiveness of treatment with removable lamellar prostheses is low with.

The use of dental implants in modern dentistry greatly contributes to the improvement of the effectiveness of orthopedic rehabilitation of patients with the loss of teeth. Tooth loss caused by periodontal disease, in patients with diabetes which makes it difficult to use them with dental implants [24,25].

Currently, one of the pressing problems of implantology is increasing the efficiency of implantation in patients at risk.

There are conflicting opinions in current scientific publications regarding the long-term survival of implants in patients with diabetes. Some authors note the normal effectiveness of treatment in diabetics, some authors take the opposite point of view, stating a low percentage of osseointegration of implants compared to the same indicators in practically healthy individuals [26,27]. These authors consider the use of implants in patients with diabetes mellitus as a relative contraindication due to systemic disorders of bone metabolism, which slow down the process of osseointegration of the implant and increase the likelihood of peri-implantitis [28,29].

Analysis of findings from animal models with hyperglycemia has shown decreased osseointegration as bone healing around dental implants is impaired [30-33].

One of the methods for improving the efficiency of osseointegration in patients with diabetes mellitus is lower, using UV photo functionalization of implants, which changes the physicochemical properties of titanium implants, transforming titanium surfaces from hydrophobic to superhydrophilic [34-39].

Experimental studies show the beneficial effects of UV-treated titanium implants in animal models, but little information is available on the effects of UV exposure on titanium implants used in diabetic patients [40].

UV radiation enhances bone morphogenesis around implants and can be an effective measure to improve implant therapy in patients with diabetes mellitus [41,43].

Clarifying these problems and developing optimal methods for the prevention and treatment of peri-implantitis in diabetics are very important from both a practical and scientific point of view, which requires long-term research.

Along with bone metabolism disorders, vitamin D disorders are also observed in patients with type 2 diabetes, hypovitaminosis D is very common in this category of patients [43,44].

Vitamin D3 is the main form of the vitamin D family and is activated by hydroxylation in the liver [45,46].

Vitamin D3 is produced in the skin from 7-dehydrocholesterol under the action of UV radiation, which splits ring B with the formation of primary D [47]. Vitamin D is also contained in small amounts in the diet. Liver and other tissues convert vitamin D from skin or food [48].

Vitamin D stimulates osteoclastic activity and production of extracellular matrix proteins by osteoblasts [45]. Moreover, it increases the absorption of calcium in the intestines.

According to the report of international experts deficiency of vitamin D is defined as any level in blood serum from 21 to 29 ng/ml [49].

In addition, the genetic polymorphism of vitamin D can lead to the violation of glycemic control [50].

Vitamin D affects the modulation of the immune system, increases the production of cathelicidin and defensin and reduces the production of pro-inflammatory cytokines, modulates the activity of lymphocytes, has a positive effect on bone metabolism [51].

Vitamin D most obvious function, i.e. regulation of calcium, homeostasis and bone metabolism, it affects the differentiation of cells, especially important is the influence of vitamin D on a number of processes of the immune system, it also participates in the regulation of insulin secretion [52].

Vitamin D is involved in the regulation of calcium and phosphate balance, which is necessary for proper mineralization of bones [54].

Hypocalcemia in the blood stimulates the secretion of parathyroid hormone, which enhances the absorption of calcium from the bones. This leads to osteomalacia or osteoporosis. Therefore, the role of vitamin D in regulating calcium balance is extremely important [52,53].

Although the function of vitamin D in regulating blood glucose levels is still not fully understood, vitamin D status appears to play a role in the development and treatment of diabetes [50,55].

Most studies examining the effects of vitamin D on glucose metabolism have supported the hypothesis that adequate vitamin D supplementation can improve metabolic regulation of glucose levels in type 2 diabetes [56].

Along with many other factors, vitamin D also influences various stages of osseointegration of endosseous implants [57].

Adequate vitamin D concentrations correlate with success at each stage of implant osseointegration [58].

The first period after implantation is significantly dependent on the role of vitamin D, it reduces the level of pro-inflammatory cytokines, thereby reducing the body's response to surgery [59].

Based on the available literature, it can be concluded that there is a relationship between vitamin D concentration and the process of osseointegration [60,61].

During osseointegration, vitamin D influences the differentiation processes of osteoblasts and osteoclasts [62]. Vitamin D has also been found to be essential for the maturation and proper functioning of bone cells. Vitamin D also increases the mineralization of osteoid cells [63,64].

This mechanism also plays an important role during the osseointegration phase of the implant.

Vitamin D supplementation improves osseointegration in animals with systemic diseases such as diabetes mellitus and osteoporosis. Little evidence supports the hypothesis that humans obtain similar benefits from vitamin D supplementation in terms of osseointegration. Further research is needed to confirm these assumptions [65].

The true influence of diabetes and hyperglycemia on peri-implantitis and implant rejection is still uncertain, and new studies are needed on larger groups of patients, also taking into account such important parameters as initial and subsequent HbA1c values, duration of diabetes, and long-term treatment. The term glycemia and levels of HbA1c. Interrelationship between changes and state of health of tissues around the implant [66].

Monitoring of key parameters of glycemic control is desirable not only for research purposes, but also for clinicians, since poor metabolic control can lead to such complications as increased risk of infections. Strict and intensive glycemic control in patients with diabetes can delay the occurrence and progression of many microvascular disorders, which are an important risk factor for peri-implantitis.

Although it has been proven that diabetes is an important risk factor for the development of peri-implantitis [67,68] one of the urgent tasks of dental science is to review the list of contraindications to implantation and consider patients with diabetes as candidates for dental implantation.

Animal experiments have shown the benefits of vitamin D supplementation to have a positive effect on implant osseointegration [60,61].

However, several clinical studies have shown conflicting results linking vitamin D to osseointegration success [69-71]. There is little evidence to support the positive benefit of vitamin D supplementation on osseointegration [65].

A review of the literature shows that the effectiveness of vitamin supplements on the osseointegration of implants in patients with diabetes has not been sufficiently studied, and the question remains whether vitamin D supplements are useful for osseointegration.

The answer to this question can be given by a multicenter independent study on numerous patients with implants, which is planned to be carried out by the author of this review.

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#### Statement of authorship:

**HKh:** contributed to design, analysis and interpretation, and drafted the manuscript. critically revised the manuscript, final wrote.

#### References

1. Tafuri G, Santilli M, Manciocchi E, Rexhepi I, D'Addazio G, et al. A systematic review on removal of osseointegrated implants: An update. *BMC Oral Health*. 2023; 23: 756.
2. Michael Alterman Ole T, Jensen Paul L, Glick Dor Mazor, Nardy Casap. Dental implant risk factors for peri-implant disease: A narrative review. *Front of oral and maxillofacial medicine*. 2023; 5: 26. <https://dx.doi.org/10.21037/fomm>
3. Polymeri A, Loos BG, Aronovich S, et al. Risk factors, diagnosis, and treatment of peri-implantitis: A cross-cultural comparison of U.S. and European periodontists' considerations. *J Periodontol*. 2022; 93: 481-492.
4. Anderson N, Lords A, Laux R, et al. Retrospective Analysis of the Risk Factors of Peri-implantitis. *J Contemp Dent Pract*. 2020; 21: 1350-1353.
5. Kochar SP, Reche A, Paul P. The Etiology and Management of Dental Implant Failure: A Review. *Cureus*. 2022; 14: e30455.
6. Kourtis SG, Sotiriadou S, Voliotis S, Challas A. Private practice results of dental implants. Part I: Survival and evaluation of risk factors--Part II: Surgical and prosthetic complications. *Implant Dent*. 2004; 13: 373-385.
7. Monje A, Alcoforado G, Padiar-Molina M, Suarez F, Lin GH, et al. Generalized aggressive periodontitis as a risk factor for dental implant failure: a systematic review and meta-analysis. *J Periodontol*. 2014; 85: 1398-1407.
8. Kim KK, Sung HM. Outcomes of dental implant treatment in patients with generalized aggressive periodontitis: A systematic review. *J Adv Prosthodont*. 2012; 4: 210-7.
9. Al Ansari Y, Shahwan H, Chrcanovic BR. Diabetes Mellitus and Dental Implants: A Systematic Review and Meta-Analysis. *Materials (Basel)*. 2022; 15: 3227.
10. Wagner J, Spille JH, Wiltfang J, Naujokat H. Systematic review on diabetes mellitus and dental implants: An update. *Int J Implant Dent*. 2022; 8: 1.
11. Moraschini V, Barboza ES, Peixoto GA. The impact of diabetes on dental implant failure: A systematic review and meta-analysis. *Int J Oral Maxillofac Surg*. 2016; 45: 1237-1245.
12. Dubey RK, Gupta DK, Singh AK. Dental implant survival in diabetic patients; Review and recommendations. *Natl J Maxillofac Surg*. 2013; 4: 142-150.
13. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care*. 1998; 21: 1414-1431.
14. Karnchanasorn R, Huang J, Ou HY, et al. Comparison of the Current Diagnostic Criterion of HbA1c with Fasting and 2-Hour Plasma Glucose Concentration. *J Diabetes Res*. 2016; 2016: 6195494.
15. American Diabetes Association Professional Practice Committee. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2022. *Diabetes Care*. 2022; 45: S17-S38.
16. Murray CE, Coleman CM. Impact of Diabetes Mellitus on Bone Health. *Int J Mol Sci*. 2019; 20: 4873.

17. Mauri-Obradors E, Estrugo-Devesa A, Jané-Salas E, Viñas M, López-López J, et al. Oral manifestations of Diabetes Mellitus. A systematic review. *Med Oral Patol Oral Cir Bucal*. 2017; 22: e586-e594.
18. Albert DA, Ward A, Allweiss P, Graves DT, Knowler WC, et al. Diabetes and oral disease: Implications for health professionals. *Ann N Y Acad Sci*. 2012; 1255: 1–15.
19. Sanjeeta N, Sivapatha sundharam B, Nandini DB. Oral lesions and periodontal status in diabetics and non-diabetics: A hospital based study. *J Oral Maxillofac Pathol*. 2022; 26: 419.
20. Ahmadinia AR, Rahebi D, Mohammadi M, Ghelichi-Ghojogh M, Jafari A, et al. Association between type 2 diabetes (T2D) and tooth loss: a systematic review and meta-analysis. *BMC Endocr Disord*. 2022; 22: 100.
21. Weijndijk LPM, Ziukaite L, Van der Weijden GAF, Bakker EWP, Slot DE, et al. The risk of tooth loss in patients with diabetes: A systematic review and meta-analysis. *Int J Dent Hyg*. 2022; 20: 145-166.
22. Wiener RC, Shen C, Findley PA, Sambamoorthi U, Tan X. The association between diabetes mellitus, sugar-sweetened beverages, and tooth loss in adults: Evidence from 18 states. *J. Am. Dent. Assoc*. 2017; 148: 500–509.e4.
23. Radović K, Obradović-Djuričić K, Čairović A, Glišić M, Djurišić S, et al. Prosthetic treatment after teeth extractions in patients with type 2 diabetes mellitus. *Srp Arh Celok Lek*. 2016; 144: 474-477.
24. Al Ansari Y, Shahwan H, Chrcanovic BR. Diabetes Mellitus and Dental Implants: A Systematic Review and Meta-Analysis. *Materials (Basel)*. 2022; 15: 3227.
25. Wagner J, Spille JH, Wiltfang J, Naujokat H. Systematic review on diabetes mellitus and dental implants: an update. *Int J Implant Dent*. 2022; 8: 1.
26. Moraschini V, Barboza ES, Peixoto GA. The impact of diabetes on dental implant failure: a systematic review and meta-analysis. *Int J Oral Maxillofac Surg*. 2016; 45: 1237–1245.
27. Dubey RK, Gupta DK, Singh AK. Dental implant survival in diabetic patients; review and recommendations. *Natl J Maxillofac Surg*. 2013; 4: 142-150.
28. Naujokat H, Kunzendorf B, Wiltfang J. Dental implants and diabetes mellitus—a systematic review. *Int J Implant Dent*. 2016; 2: 5.
29. Al Amri MD, Kellesarian SV, Ahmed A, et al. Efficacy of peri-implant mechanical debridement with and without adjunct antimicrobial photodynamic therapy in patients with type 2 diabetes mellitus. *Photodiagnosis Photodyn Ther*. 2016; 14: 166-169.
30. Tan SJ, Baharin B, Mohd N, Nabil S. Effect of Anti-Diabetic Medications on Dental Implants: A Scoping Review of Animal Studies and Their Relevance to Humans. *Pharmaceuticals (Basel)*. 2022; 15: 1518.
31. Dubey RK, Gupta DK, Singh AK. Dental implant survival in diabetic patients; review and recommendations. *Natl. J. Maxillofac. Surg*. 2013; 4: 142–150.
32. Shang R, Gao L. Impact of hyperglycemia on the rate of implant failure and peri-implant parameters in patients with type 2 diabetes mellitus: Systematic review and meta-analysis. *J. Am. Dent. Assoc*. 2021; 152: 189–201.e1.
33. Wagner J, Spille JH, Wiltfang J, Naujokat H. Systematic review on diabetes mellitus and dental implants: An update. *Int. J. Implant. Dent*. 2022; 8: 1.
34. Kheur S, Kheur M, Madiwal V, Sandhu R, Lakha T, et al. In-Vitro Evaluation of Photo functionalized Implant Surfaces in a High-Glucose Microenvironment Simulating Diabetics. *J Funct Biomater*. 2023; 14: 130.
35. Aita H, Hori N, Takeuchi M, Suzuki T, Yamada M, et al. The effect of ultraviolet functionalization of titanium on integration with bone. *Biomaterials*. 2009; 30: 1015–1025.
36. Gröbe A, Heiland M, Ebker T. Impact of Dental Implant Surface Modifications on Osseointegration. *Biomed Res. Int*. 2016; 2016: 6285620.
37. Dini C, Nagay BE, Magno MB, Maia LC, Barão VAR, et al. Photo-functionalization as a suitable approach to improve the osseointegration of implants in animal models—A systematic review and meta-analysis. *Clin. Oral Implants Res*. 2020; 31: 785–802.
38. Funato A, Yamada DDSM, Ogawa T. Success Rate, Healing Time, and Implant Stability of Photofunctionalized Dental Implants. *Int. J. Oral Maxillofac. Implants*. 2013; 28: 1261–1271.
39. Funato A, Ogawa T. Photo functionalized Dental Implants: A Case Series in Compromised Bone. *Int. J. Oral Maxillofac. Implants*. 2013; 28: 1589–1601.
40. Sugita Y, Honda Y, Kato DDSI. Role of Photo functionalization in Mitigating Impaired Osseointegration Associated with Type 2 Diabetes in Rats. *Int. J. Oral Maxillofac. Implants*. 2014; 29: 1293–1300.
41. Hirakawa Y, Jimbo R, Shibata Y, Watanabe I, Wennerberg A, et al. Accelerated bone formation on photo-induced hydrophilic titanium implants: An experimental study in the dog mandible. *Clin. Oral Implants Res*. 2013; 24: 139–144.
42. Ikeda T, Okubo T, Saruta J, Hirota M, Kitajima H, et al. Osteoblast attachment compromised by high and low temperature of titanium and its restoration by UV photofunctionalization. *Materials*. 2021; 14: 5493.
43. Karau PB, Kirna B, Amayo E, Joshi M, Ngare S, et al. The prevalence of vitamin D deficiency among patients with type 2 diabetes seen at a referral hospital in Kenya. *Pan Afr Med J*. 2019; 34: 38.
44. Strange RC, Shipman KE, Ramachandran S. Metabolic syndrome: A review of the role of vitamin D in mediating susceptibility and outcome. *World J Diabetes*. 2015; 6: 896-911.
45. Bikle DD. Vitamin D metabolism, mechanism of action, and clinical applications. *Chem Biol*. 2014; 21: 319-329.
46. Fleet JC. The role of vitamin D in the endocrinology controlling calcium homeostasis. *Mol Cell Endocrinol*. 2017; 453: 36-45.
47. Taylor CL, Rosen CJ, Dwyer JT. Considerations in dietetic counseling for vitamin D. *J Acad Nutr Diet* 2019; 119: 901-909.
48. Agency for Healthcare Research and Quality. Screening for vitamin D deficiency: Systematic review for the U.S. Preventive Services Task Force recommendation. Evidence Synthesis Number 118. AHRQ-Pub No. 13-05183-EF-1. June 2014.
49. Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Köstenberger M, et al. Vitamin D deficiency 2.0: An update on the current status worldwide. *Eur J Clin Nutr*. 2020; 74: 1498-1513.
50. Abugoukh TM, Al Sharaby A, Elshaikh AO, Joda M, Madni A, et al. Does Vitamin D Have a Role in Diabetes? *Cureus*. 2022; 14: e30432.
51. Kamen DL, Tangpricha V. Vitamin D and molecular actions on the immune system: modulation of innate and autoimmunity. *J Mol Med (Berl)*. 2010; 88: 441-450.

52. Fleet JC. The role of vitamin D in the endocrinology controlling calcium homeostasis. *Mol Cell Endocrinol.* 2017; 453: 36-45.
53. Khazai N, Judd SE, Tangpricha V. Calcium and vitamin D: skeletal and extraskeletal health. *Curr Rheumatol Rep.* 2008; 10: 110-117.
54. Laird E, Ward M, McSorley E, Strain JJ, Wallace J. Vitamin D and bone health: Potential mechanisms. *Nutrients.* 2010; 2: 693-724.
55. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J Clin Endocrinol Metab.* 2007; 92: 2017-29.
56. Tang H, Li D, Li Y, Zhang X, Song Y, et al. Effects of Vitamin D Supplementation on Glucose and Insulin Homeostasis and Incident Diabetes among Nondiabetic Adults: A Meta-Analysis of Randomized Controlled Trials. *Int J Endocrinol.* 2018; 2018: 7908764.
57. Makke A. Vitamin D Supplementation for Prevention of Dental Implant Failure: A Systematic Review. *Int J Dent.* 2022; 2022: 2845902.
58. Salomo-Coll O, Mate-Sanchez de Val J, Ramirez-Fernandez M, Hernandez-Alfaro F, Gargallo-Albiol J, et al. Topical Applications of Vitamin D on Implant Surface for Bone to Implant Contact Enhance: A Pilot Study in Dogs Part 2. *Clinical Oral Implants Research.* 2015; 27: 896-903. <https://doi.org/10.1111/clr.12707>
59. Akhavan A, Noroozi Z, Shafiei AA, Haghghat A, Jahanshahi GR, et al. The effect of vitamin D supplementation on bone formation around titanium implants in diabetic rats. *Dent Res J (Isfahan)* 2012; 9: 582-587.
60. Dvorak G, Fügl A, Watzek G, Tangl S, Pokorny P, et al. Impact of Dietary Vitamin D on Osseointegration in the Ovariectomized Rat. *Clinical Oral Implants Research.* 2012; 23: 1308-1313. <https://doi.org/10.1111/j.1600-0501.2011.02346.x>
61. Werny JG, Sagheb K, Diaz L, Kämmerer PW, Al-Nawas B, et al. Does vitamin D have an effect on osseointegration of dental implants? A systematic review. *Int J Implant Dent.* 2022; 8: 16.
62. van Driel M, van Leeuwen JP. Vitamin D endocrine system and osteoblasts. *Bonekey Rep.* 2014; 3: 493.
63. Laird E, Ward M, McSorley E, Strain JJ, Wallace J. Vitamin D and bone health: Potential mechanisms. *Nutrients.* 2010; 2: 693-724.
64. Wacker M, Holick MF. Vitamin D - effects on skeletal and extraskeletal health and the need for supplementation. *Nutrients.* 2013; 5: 111-148.
65. Markopoulos G, Lepetsos P, Perrea DN, Iliopoulos DC, Nikolaou VS, et al. Possible Roles of Vitamin D in Bone Grafting. *Cureus.* 2021; 13: e14688.
66. Alberti A, Morandi P, Zotti B, Tironi F, Francetti L, et al. Influence of Diabetes on Implant Failure and Peri-Implant Diseases: A Retrospective Study. *Dent J (Basel).* 2020; 8: 70.
67. Dioguardi M, Cantore S, Quarta C, Sovereto D, Zerman N, et al. Correlation between Diabetes Mellitus and Peri-implantitis: A Systematic Review. *EndocrMetab Immune Disord Drug Targets.* 2023; 23: 596-608.
68. Shang R, Gao L. Impact of hyperglycemia on the rate of implant failure and peri-implant parameters in patients with type 2 diabetes mellitus: Systematic review and meta-analysis. *J Am Dent Assoc.* 2021; 152: 189-201.e1.
69. Cantorna MT, Snyder L, Lin YD, Yang L. Vitamin D and 1, 25(OH)2D Regulation of T Cells. *Nutrients.* 2015; 7: 3011-3021. <https://doi.org/10.3390/nu7043011>
70. Hansen KE. Osteoimmunology: Prevalence of Hypovitaminosis D and Relationship to Fracture. *Nature Reviews Rheumatology.* 2009; 5: 417-418. <https://doi.org/10.1038/nrrheum.2009.143>
71. Takayanagi H. Interaction between the Immune System and Bone Metabolism: An Emerging Field of Osteoimmunology. *The Proceedings of the Japan Academy.* 2007; 83: 136-143. <https://doi.org/10.2183/pjab.83.136>