Impact of Vitamin D Deficiency on Oral Health

Da-Ming Liao1, Chieh Chen2

Dental Department, Puli Christian Hospital, R.O.C.1

Department of family medicine, Hualien Armed Forces General Hospital, R.O.C.2

Corresponding author: Chieh Chen

Address: 970 No. 198, Minde 1st Street, Hualien city

Tel: 0928-698950

E-mail: guppy5230@yahoo.com.tw

Running title: Vitamin D Deficiency and Oral Health

Abstract

Normally, the body can produce vitamin D at sun exposure. The deficiency has been linked to a variety of diseases, including in the oral cavity. Inadequate sun exposure may accelerate the onset of these diseases since the synthesis of vitamin D is interrupted. Vitamin D not only benefits the overall health of oral cavity but is also associated with tooth mineralization. It can help to fight against inflammation and stimulate the production of antimicrobial peptides for immune response. Thus, in this paper, we will briefly discuss the origin of various oral diseases caused by insufficient level of vitamin D in the body and shed light on the potential benefits of safe sun exposure to maintain both oral and body health.

Keywords: Oral health; Vitamin D deficiency; Periodontal disease; Periodontitis; Dental caries.

**Introduction**

Studies have found that people of darker skin color with vitamin D deficiency, overweight or obesity have a higher risk of diabetes or oral diseases (periodontal disease, periodontitis and dental caries). Vitamin D is essential in maintaining the calcium homeostasis, even though it also plays an important role in immunity, cardiovascular system, diabetes, cancer, and chronic illness[1]. The primary sources of vitamin D are dietary intake and sunlight exposure in the form of vitamin D2 and D3, which are metabolized to 25-hydroxyvitamin D [25(OH)D] in the liver. The compound is activated in the kidneys in the form of 1,25-dihydroxyvitamin D. Periodontitis is characterized by alveolar bone loss induced by the host’s immune response to bacterial assault. For its crucial role in the maintenance of bone structure and immunity, it is only logical to suspect its deficiency will negatively affect the periodontium in the oral cavity. Vitamin D deficiency is diagnosed by the level of serum 25(OH)D, in which the normal value should fall between 20 to 75ng/mL. Although there is no accepted standard value to declare deficiency, most scholars have agreed to numbers from 20 to 30 ng/mL as mild deficiency and severe case if the value falls below 20 ng/mL (figure 1)[1-3].

**Oral Manifestation of Vitamin D Deficiency**

Vitamin D also exhibits anti-inflammatory activities and thus, its deficiency may well relate to some immune diseases, such as insulin-deficiency diabetes, rheumatoid arthritis, etc. The COVID-19 epidemic may also be associated with vitamin D insufficiency. Teeth are considered mineralized tissues, surrounded by alveolar bones, which are constituted of three different hard tissues, namely enamel, dentin, and cementum. The process of mineralization occurs simultaneously in the teeth and the bone structure. Any interruption to the process will exhibit similar symptoms of osteogenesis failure[4-10]. Vitamin D is a key player in this process and low concentration will result in an increase in dental caries. Also, the process is subjected to congenital gene defects that may also result in dental caries or corrosion (demineralization) if the teeth were not sufficiently developed. Other studies have pointed out that vitamin D can protect the oral cavity and reduce oral infection, as these bacteria do not only cause inflammation in the gums and periodontium but also can lead to tooth loss. Researchers have concluded that higher intake of vitamin D will protect from the progression of periodontal disease, despite that an earlier study, which only included calcium intake and not vitamin D, showed to slow down periodontal disease and tooth loss in males[11,12]. Without knowing the baseline concentration of 25(OH)D, it would be impossible to determine the role of vitamin D in periodontal disease. Vitamin D reduces the risk of gum inflammation, mainly through protecting the periodontium. Thus, it is speculated that by preventing inflammation and modulating the immune response in periodontium, vitamin D can affect the pathogenesis in the oral cavity. Plus, vitamin D functions to increase bone mineral density (the mandible), reduce alveolar bone resorption, and inhibit the inflammatory response associated with periodontal disease. The correlation between vitamin D and the disease is dependent of the dosage, especially when we already know that the concentration of vitamin D will affect bone stability and growth, such as in tooth. In addition to the direct impact on bone metabolism, it also indirectly helps by inhibiting pathogens in the periodontium and healing from gingivitis. Vitamin D is also known to inhibit cytokines for inflammatory response that leads to the destruction of periodontium[13-19]. Therefore, immune response is highly dependent of nutritional status of the host. Vitamin D is not only important for the prevention of periodontal disease, but also gingivitis. In fact, it can reverse the state of destruction even when the periodontal disease has already damaged the alveolar bone tissues. Vitamin D is needed to maintain healthy teeth and immune system to prevent periodontal disease, implying that malnutrition will delay the repair process of gingival damage and increase the dental space in oral cavity to permit bacterial invasion into the teeth and the marrow. The biologically active compound, 1,25(OH)2D and the vitamin D receptor will interact to maintain healthy functioning oral epithelial cells and immunity. Although the deficiency of vitamin D is rarely the sole reason to cause cancer, the risk of oral squamous cell carcinoma is dramatically increased if synergistically combined with other genetic or environmental factors. The binding of 1,25(OH)2D/VDR is most likely to maintain the metabolic balance of oral mucosal tissues and provide a protective barrier against diseases like periodontitis and dental plaques since plenty evidence has shown the deficiency to be associated with an increased risk of chronic periodontitis. Therefore, supplementing the body with bioactive vitamin D may be helpful for the general treatment of chronic periodontitis[20-25].

**Sources of Vitamin D**

Vitamin D is a fat-soluble compound in the class of steroids. 90% of vitamin D can be synthesized naturally by exposing to ultraviolet B rays through the skin. Skin color, age, and duration and area of exposure will all affect the yield. The most important function of vitamin D is to maintain the balance of calcium and phosphorus ions in the growth and reconstruction of bones[26-31]. It is also involved in regulating the functions of bones, muscles, nerves and immunity, also including the cardiovascular and endocrine systems, as well as playing a role in cell cycle. Vitamin D requires activation from substrates in the liver and kidneys to become biologically active. These active metabolites of vitamin D include Cholecalciferol (vitamin D3), Calcidiol (25-hydroxyvitamin D3), Calcitriol (1, 25-dihydroxyvitamin D3), Ergocalciferol (vitamin D2) and others. The most important of these metabolites are vitamin D2 and vitamin D3 (calciferol)[32-36].

**Oral Wound Treatment and Hygiene**

Vitamin D regulates calcium and immune function. Although the correlation between vitamin D deficiency and periodontal inflammation has been well studied, its impact on the healing of oral wound from periodontal surgery is not clear. When compared with sufficient level of vitamin D, the deficiency showed less regression of subosseous defects. Animal studies have also suggested that vitamin D is essential in anabolic bone formation in the mandible and may have a positive effect on the healing of fracture. Given its ability to heal bones in the oral cavity, the supplement of vitamin D at the time or after the surgery may benefit[37-41]. However, vitamin D deficiency is very common in the population that it is usually recommended to supplement enough vitamin D before the periodontal surgery to achieve a good prognosis. Healthy people are capable of producing vitamin D in the body after exposing to sunlight. Its deficiency has been linked to a variety of diseases, including oral diseases. And inadequate exposure to sunlight may accelerate the onset of these diseases, possibly because of insufficient vitamin D synthesis. Vitamin D is not only limited to the mineralization of teeth but also can help the body fight against inflammation and infection by stimulating the production of antimicrobial peptides. This paper would briefly discuss the origin of various oral diseases caused by the insufficient level of vitamin D in the body and shed light on the potential benefits of safe sun exposure for maintaining oral and body health. Since vitamin D deficiency is highly prevalent, it may be advisable to keep the level within the normal range in advance of periodontal surgery to get the best prognosis of treatment. Good nutrition is needed for sustaining healthy tissues, maintaining the immune system, and protecting the body against periodontal disease. Malnutrition will delay the repair process in the gingival space and increase the cell permeability, making it easier for bacteria to enter the tissues[42-48].

**Conclusion**

Statistics have shown that the average level of serum 25(OH)D appears to be declining over the past decades because of changes in BMI, dietary habit, and sun exposure. The participants under medication of Teriparatide showed linear bone growth. The deficiency of vitamin D, when compared with those with sufficient vitamin D, showed lower resolution in radiograph, which indicated periodontal infrabony defects. Animal studies suggested that vitamin D plays a crucial role in the anabolic bone formation of the mandible and may even positively affect the healing of fracture[49-51]. Moreover, vitamin D deficiency was shown to compromise the osseous healing in the oral cavity, as evidenced in the pre-clinical study of bisphosphonate-associated osteonecrosis of the jaw, further supporting the fact that vitamin D assists in the healing of bones in the oral cavity.

**Reference**

1. Khammissa RAG, Fourie J, Motswaledi MH, Ballyram R, Lemmer J, Feller L. The biological activities of vitamin D and its receptor in relation to calcium and bone homeostasis, cancer, immune and cardiovascular systems, skin biology, and oral health. BioMed research international 2018: 1-10.
2. Chou HY, Lee KF, Chang LC. Jaw Bone Lesion Associated with Vitamin D Deficiency-A Case Report. Chinese Journal of Oral and Maxillofacial Surgery 2020; 31(4): 318-25.
3. Haussler MR, Whitfield GK, Kaneko I, Haussler CA, Hsieh D, Hsieh JC, et al. Molecular mechanisms of vitamin D action. Calcified tissue international 2013; 92(2): 77-98.
4. Stein SH, Tipton DA. Vitamin D and its impact on oral health—An update. Journal of the Tennessee Dental Association 2011; 91(2): 30-6.
5. Uwitonze AM, Murererehe J, Ineza MC, Harelimana EI, Nsabimana U, Uwambaye P, et al. Effects of vitamin D status on oral health. The Journal of steroid biochemistry and molecular biology 2018; 175: 190-4.
6. Botelho J, Machado V, Proença L, Delgado AS, Mendes JJ. Vitamin D deficiency and oral health: a comprehensive review. Nutrients 2020; 12(5): 1471-3.
7. Dragonas P, El-Sioufi I, Bobetsis YA, Madianos PN. Association of vitamin D with periodontal disease: a narrative review. Oral Health Prev. Dent 2020; 18: 103-14.
8. Jimenez M, Giovannucci E, Kaye EK, Joshipura KJ, Dietrich T. Predicted vitamin D status and incidence of tooth loss and periodontitis. Public health nutrition 2014; 17(4): 844-52.
9. Öztekin A, Öztekin C. Vitamin D levels in patients with recurrent aphthous stomatitis. BMC Oral Health 2018; 18(1): 1-5.
10. Miley DD, Garcia MN, Hildebolt CF, Shannon WD, Couture RA, Anderson Spearie CL, et al. Cross‐sectional study of vitamin D and calcium supplementation effects on chronic periodontitis. Journal of periodontology 2009; 80(9): 1433-9.
11. Alzahrani AAH, Alharbi RA, Alzahrani MSA, Sindi MA, Shamlan G, Alzahrani, FA, et al. Association between periodontitis and vitamin D status: A case-control study. Saudi Journal of Biological Sciences 2021; 28(7): 4016-21.
12. Y Amano, K Komiyama, M Makishima. Vitamin D and periodontal disease. Journal of oral science 2009; 51: 11-20.
13. Bashutski JD, Eber RM, Kinney JS, Benavides E, Maitra S, Braun TM, et al. The impact of vitamin D status on periodontal surgery outcomes. Journal of dental research 2011; 90(8): 1007-12.
14. Uwitonze AM, Rahman S, Ojeh N, Grant WB, Kaur H, Haq A, et al. Oral manifestations of magnesium and vitamin D inadequacy. The Journal of steroid biochemistry and molecular biology 2020; 200: 105636.
15. Dietrich T, Garcia RI. Associations between periodontal disease and systemic disease: evaluating the strength of the evidence. Journal of periodontology 2005; 76: 2175-84.
16. Fathi N, Ahmadian E, Shahi S, Roshangar L, Khan H, Kouhsoltani M, et al. Role of vitamin D and vitamin D receptor (VDR) in oral cancer. Biomedicine & Pharmacotherapy 2019; 109: 391-401.
17. Krall EA, Wehler C, Garcia RI, Harris SS, Dawson-Hughes B. Calcium and vitamin D supplements reduce tooth loss in the elderly. The American journal of medicine 2001; 111(6): 452-6.
18. Hujoel PP, Lingström P. Nutrition, dental caries and periodontal disease: a narrative review. Journal of clinical periodontology 2017; 44: S79-S84.
19. Ciur MDI, Zetu IN, Danisia HABA, Bourgeois D, Andrian S. Evaluation of the influence of local administration of vitamin D on the rate of orthodontic tooth movement. The Medical-Surgical Journal 2016; 120(3): 694-9.
20. Cetrelli L, Bletsa A, Lundestad A, Gil EG, Fischer J, Halbig J, et al. Vitamin D, oral health, and disease characteristics in juvenile idiopathic arthritis: a multicenter cross-sectional study. BMC oral health 2022, 22(1): 1-14.
21. Antonenko O, Bryk G, Brito G, Pellegrini G, Zeni SN. Oral health in young women having a low calcium and vitamin D nutritional status. Clinical oral investigations 2015; 19(6): 1199-1206.
22. Alvarez JA, Ashraf A. Role of vitamin D in insulin secretion and insulin sensitivity for glucose homeostasis. Int J Endocrinol. 2010; 2010: 351385.
23. Schwalfenberg, G. Vitamin D and diabetes. Can Fam Physician. 2008; 54(6): 864-6.
24. Berridge MJ. Vitamin D deficiency and diabetes. Biochem J. 2017; 474(8): 1321-32.
25. Mathieu C, Gysemans C, Giulietti A, Bouillon R. Vitamin D and diabetes. Diabetologia 2005; 48: 1247-57.
26. Baz-Hecht M, Goldfine AB. The impact of vitamin D deficiency on diabetes and cardiovascular risk. Current Opinion in Endocrinology, Diabetes and Obesity 2010; 17(2): 113-9.
27. Ozfirat Z, Chowdhury TA. Vitamin D deficiency and type 2 diabetes. Postgraduate medical journal 2010; 86(1011): 18-25.
28. Svoren BM, Volkening LK, Wood JR, Laffel LM. Significant vitamin D deficiency in youth with type 1 diabetes mellitus. The Journal of pediatrics 2009; 154(1): 132-4.
29. Danescu LG, Levy S, Levy J. Vitamin D and diabetes mellitus. Endocrine 2009, 35: 11-17.
30. Palomer X, González‐Clemente JM, Blanco‐Vaca F, Mauricio D. Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. Diabetes, Obesity and Metabolism 2008; 10(3): 185-97.
31. Alloubani A, Akhu-Zaheya L, Samara R, Abdulhafiz I, Saleh A, Altowijri A. Relationship between vitamin D deficiency, diabetes, and obesity. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2019; 13(2): 1457-61.
32. Bener A, Alsaied A, Al-Ali M, Al-Kubaisi A, Basha B, Abraham A, et al. High prevalence of vitamin D deficiency in type 1 diabetes mellitus and healthy children. Acta diabetologica 2009; 46: 183-9.
33. Li YX, Zhou L. Vitamin D deficiency, obesity and diabetes. Cellular and Molecular Biology 2015; 61(3): 35-8.
34. Mathieu C, Badenhoop K. Vitamin D and type 1 diabetes mellitus: state of the art. Trends in Endocrinology & Metabolism 2005; 16(6): 261-6.
35. Holick MF. Diabetes and the vitamin D connection. Current diabetes reports 2008; 8(5): 393-8.
36. Mitri J, Pittas AG. Vitamin D and diabetes. Endocrinology and Metabolism Clinics 2014; 43(1): 205-32.
37. Takiishi T, Gysemans C, Bouillon R, Mathieu C. Vitamin D and diabetes. Rheumatic Disease Clinics 2012; 38(1): 179-206.
38. Mathieu C. Vitamin D and diabetes: where do we stand? Diabetes research and clinical practice 2015; 108(2): 201-9.
39. Penckofer S, Kouba J, Wallis DE, Emanuele MA. Vitamin D and diabetes. The Diabetes Educator 2008; 34(6): 939-54.
40. Mathieu C. Vitamin D and diabetes: where do we stand? Diabetes research and clinical practice 2015; 108(2): 201-9.
41. Martin T, Campbell RK. Vitamin D and diabetes. Diabetes spectrum 2011; 24(2): 113-8.
42. Seshadri KG, Tamilselvan B, Rajendran A. Role of vitamin D in diabetes. Journal of Endocrinology and Metabolism 2011; 1(2): 47-56.
43. Mezza T, Muscogiuri G, Sorice GP, Prioletta A, Salomone E, Pontecorvi A, et al. Vitamin D deficiency: a new risk factor for type 2 diabetes. Annals of Nutrition and Metabolism 2012; 61(4): 337-48.
44. Lips P, Eekhoff M, van Schoor N, Oosterwerff M, de Jongh R, Krul-Poel Y, et al. Vitamin D and type 2 diabetes. The Journal of steroid biochemistry and molecular biology 2017; 173: 280-5.
45. Griz LHM, Bandeira F, Gabbay MAL, Dib SA, Carvalho EFD. Vitamin D and diabetes mellitus: an update 2013. Arquivos Brasileiros de Endocrinologia & Metabologia 2014; 58: 1-8.
46. Pittas AG, Dawson-Hughes B. Vitamin D and diabetes. The Journal of steroid biochemistry and molecular biology 2010; 121(1-2): 425-9.
47. Shehab D, Al‐Jarallah K, Mojiminiyi OA, Al Mohamedy H, Abdella NA. Does Vitamin D deficiency play a role in peripheral neuropathy in Type 2 diabetes? Diabetic medicine 2012; 29(1): 43-9.
48. Botelho J, Machado V, Proença L, Delgado AS, Mendes JJ. Vitamin D deficiency and oral health: a comprehensive review. Nutrients 2020; 12(5): 1471.
49. Pittas AG, Dawson-Hughes B, Sheehan P, Ware JH, Knowler WC, Aroda VR, et al. Vitamin D supplementation and prevention of type 2 diabetes. N Engl J Med. 2019; 381(6): 520-30.
50. Mirhosseini N, Vatanparast H, Mazidi M, Kimball SM. Vitamin D supplementation, glycemic control, and insulin resistance in prediabetics: a meta-analysis. Journal of the Endocrine Society 2018; 2(7): 687-709.
51. Mirhosseini N, Vatanparast H, Mazidi M, Kimball SM. The effect of improved serum 25-hydroxyvitamin D status on glycemic control in diabetic patients: a meta-analysis. The Journal of Clinical Endocrinology & Metabolism 2017; 102(9): 3097-110.



Fig 1. The function of vitamin D.