



Effects of vitamin D status on oral health



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ABSTRACT

Normal humans of all ages have the innate ability to produce vitamin D following sunlight exposure. Inadequate vitamin D status has shown to be associated with a wide variety of diseases, including oral health disorders. Insufficient sunlight exposure may accelerate some of these diseases, possibly due to impaired vitamin D synthesis. The beneficial effects of vitamin D on oral health are not only limited to the direct effects on the tooth mineralization, but are also exerted through the anti-inflammatory functions and the ability to stimulate the production of anti-microbial peptides. In this article, we will briefly discuss the genesis of various oral diseases due to inadequate vitamin D level in the body and elucidate the potential benefits of safe sunlight exposure for the maintenance of oral and general health.

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1. Introduction

Our understanding of bioactivities of vitamin D has improved in the last two decades. The optimal vitamin D synthesis and its turnover are essential for physiological functions of almost all the systems of the body [1]. Vitamin D is a multifunctional hormone that is mostly produced in the skin following exposure to ultraviolet (UV) B sunlight. A negligible amount comes from exogenous sources (foods and supplements). Despite vitamin D synthesis is molecularly well-regulated in a limited numbers of organs, it can reach to the distant organs through the circulatory system and act on most of the cells due to presence of vitamin D receptors (VDR). It coordinates the physiological functions by controlling calcium and phosphate metabolism, promotes growth, and induces necessary remodeling of the bones and teeth [2]. The important role of vitamin D in the regulation of musculoskeletal health by maintaining mineral ion homeostasis is elaborated elsewhere [3–11]. Studies have shown that deficiency of vitamin D

may place subjects at risk, not only for low bone mineral density, osteoporosis or osteopenia but also by promoting infectious and inflammatory diseases [12,13]. Of relevance, an association between tooth loss and alveolar bone density or osteoporosis have been documented, suggesting that low bone mass is a risk factor for the evolvement of periodontal diseases [14–16]. Moreover, vitamin D may exert beneficial effects on oral health by influencing the production of anti-microbial peptides [17].

Inadequate vitamin D status in the body can induce dentin and enamel defects during tooth development, and may also increase the incidence of dental caries. In a systematic review of controlled clinical trials that included 2827 children has reported vitamin D as a promising caries-preventive agent; such results led to a low-certainty conclusion that vitamin D may reduce the incidence of caries [18]. Recently, dietary phosphorus burden has shown to increase dental caries, independent of vitamin D uptake [19]. Studies have shown that excessive intake of fatty foods may lead to both obesity and periodontal diseases in children and adolescents, whereas foods rich in riboflavin, fiber, calcium and vitamin D help in reducing the risk of gingivitis [20,21]. Using Hill's criteria for causality in a biological system, a strong inverse correlation between serum 25(OH)D and periodontal diseases was noted in a cross-sectional cohort; it was also noted that periodontal diseases

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were consistently more prevalent in darker skinned people than in lighter skinned people [22]. From the above-mentioned evidences, it is clear that continual sufficiency of vitamin D, whether derived from exogenous sources or through endogenous production, is important to preserve periodontal health. Of particular importance, more than 80% of vitamin D is generated in the skin following exposure to sunlight, (hypovitaminosis D status usually reflects reduced sunlight exposure).

2. Sunlight and vitamin D synthesis

Vitamin D synthesis is triggered in the skin following UVB ray (wavelength of 290–320 nanometers) exposure to the sunlight. Cutaneous 7-dehydrocholesterol is converted to previtamin D3 which then undergoes hydroxylation in the 25 position by the enzyme 25-hydroxylase in the liver, and results in the formation of 25-hydroxyvitamin D [25(OH)D] [3,23,24]. In plasma, 25(OH)D is the major circulating metabolite of vitamin D, and is commonly measured to provide an index of nutritional status of vitamin D, which has a circulating half-life of about 15 days [25]. It is however important to mention that plasma 25(OH)D level does not accurately reflect the amount of vitamin D present in the adipose tissues. Such accumulation of the lipophilic vitamin D molecule in the adipose tissue can reduce its bioavailability [26,27]. A second hydroxylation then takes place in the kidney to generate the biologically active form of 1,25-dihydroxyvitamin D [1,25(OH)2D] [3]. The presence of VDR in most tissues raises the possibility of a broad biological function for vitamin D, beyond calcium and phosphate metabolism. In fact, studies have shown a vital role of vitamin D—ranging from cell growth to immune regulation to inflammatory modulation (Fig. 1) [28–33].

The adverse consequence of inadequate level of vitamin D is well documented in skeletal diseases, including rickets (in children) and osteomalacia (in adults). According to Institute of Medicine (IOM), 25(OH)D levels of ≥ 20 ng/mL are considered sufficient, and 12 ng/mL or less are considered as vitamin D deficiency state—while serum levels >50 ng/mL could exert potential harmful effects. It is important to note that the IOM recommended values are considered too low by some professionals involved in vitamin D treatment, and proposed >75 nmol/L

as desirable [34]. A relatively large study conducted on 247,574 patients showed an increased risk of all-causes for mortality (HR 1.42, 95%CI 1.31–1.52) in patients who have 25(OH)D levels above the range of 50–60 nmol/L. These authors concluded that 20 to 24 ng/mL is the optimal level [35], which is around the IOM recommendation range. Of relevance, 'U'-shaped association of vitamin D and health outcome is an unsettled issue [36]. Since the purpose of this article is to discuss the role of vitamin D on oral health, deliberating the longstanding debate of IOM recommendation levels, and whether disease association with vitamin D is 'U'-shaped or 'J'-shaped are beyond the scope of this article [37].

A full body exposure to the sun for around 30 min can generate almost 10,000 units of vitamin D in humans [38]. Several factors influence sunlight-induced vitamin D synthesis including state of skin pigmentation, and geographical locations (e.g., higher latitude) [39]. For instance, a much higher baseline levels of serum 25(OH)D is detected in many African countries, as compared to the countries of other continents. For instance, in a study of 113 Gambian women aged 45–80 years, the mean 25(OH)D level was 91 nmol/L, and there was no association with different age groups (Table 1). In Cameroon, 152 men and women over 60 years, the mean 25(OH)D concentration was around 52 nmol/L. Vitamin D status in the indigenous populations of Tanzania showed that the mean 25(OH)D was around 106 nmol/L in non-pregnant women and around 138 nmol/L in pregnant women [40]. Such higher levels of 25(OH)D in African countries are likely to be related to exposure to sunlight. National Health and Nutrition Examination Surveys (NHANES) found that serum 25(OH)D levels were higher during the summer (May to October), compared to the other months of the year in the USA, perhaps due to more exposure to sunlight during summer (for more outdoor activities). African women of Maasai and Hadzabe origin had higher 25(OH)D compared to women of Sengerema origin who cover all but their lower arms and faces [40], clearly suggesting that exposure to sunlight (rather than dietary intake) is principal determinant of vitamin D status in the body. Of clinical importance, low sun exposure has shown to be associated with increased risk of cardiovascular diseases and brain disorders [41–49]. Sunlight exposure can also help reduce blood pressure, possibly by increasing the production of 1,25(OH)2D [50–52]. In a similar line of observation, cancer-related death rates decline in the lower latitudes where sunshine is more abundant [53–55]. An inverse relationship exists between periodontal disease and the amount of vitamin D intake, and when available, a safe sunlight exposure should be encouraged to improve vitamin D status to reduce oral disease burden.

3. Vitamin D and oral health

Deficiency of vitamin D is a major risk factor for the genesis of osteoporosis, which may also affect the functionality of the jaws [56]. In a longitudinal study, conducted on 562 elderly men, daily intake of total vitamin D was associated with better periodontal health, as measured through alveolar bone loss, pocket depth, and attachment loss. Total vitamin D intake ≥ 800 IU was associated with lower odds of severe periodontal disease (OR=0.67, 95% CI=0.55–0.81) and moderate-to-severe alveolar bone loss (OR=0.54, 95% CI=0.30–0.96) relative to intake <400 IU/day [56]. The investigators concluded that intake of higher vitamin D may exert protective function against the progression of the periodontal diseases. Although, in an earlier study, only calcium intake – not vitamin D, was found to help to decrease the progression of the periodontal diseases and tooth loss in men [57]; it is however relevant to mention that without knowing baseline 25(OH)D concentration, it is not possible to determine what the effect of vitamin D is on periodontal diseases [58].

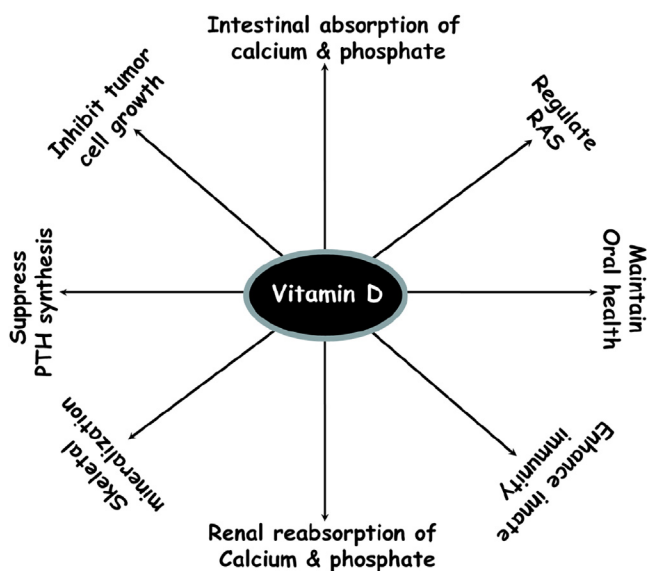


Fig. 1. The vitamin D is a multifunctional hormone and can exert numerous essential functions beyond skeletal system. For keeping the figure simple, the main functions of vitamin D are listed in the figure. RAS: renin-angiotensin system, PTH: Parathyroid hormone.

Table 1
Vitamin D status in various African countries, compiled from earlier published articles [40,85].

No	Location	Study group	Age	Mean 25 (OH)D level
1	Gambia	113 women	45–80 yrs	91.2 nmol/L
2	Cameroon	152 men & women	Over 60 yrs	52.7 nmol/L
3	Tanzania	Indigenous population (pregnant)	Not specified	138.5 nmol/L
		Indigenous population (non-pregnant)	Not specified	106.8 nmol/L
4	South Africa	Black African	>65 yrs	37 nmol/L; 17% has level under 25 nmol/L

An analysis of cross-sectional data from the third NHANES showed that individuals with the highest 25(OH)D levels experienced 20% less bleeding on probing than those with the lowest levels- maintaining the optimal level of vitamin D in the body is likely to reduce the risk of evolvement of gingivitis by exerting anti-inflammatory effects [59]. A longitudinal study that was conducted on individuals with sufficient and insufficient vitamin D to assess the outcomes of periodontal surgery; Teriparatide administration showed that minimal benefits was obtained from periodontal surgery done on individuals deficient in vitamin-D. A strong relationship exists between skeletal bone density with periodontal health and osteointegrated implant success [60,61]. Inadequate level of vitamin D in individuals has been reported to be associated with hypoplasia of the enamel and atrophy of the salivary glands, and thereby facilitates development of dental caries [62]. From the results obtained from a study conducted on pre-school children, Schroth et. calculated that caries-free children were twice as likely to have 25(OH)D concentrations around the range of ≥ 75 nmol/L, while those with severe caries were three times more likely to have 25(OH)D concentrations around < 35 nmol/L [63].

Both human and experimental studies have shown an association between inadequate status of vitamin D and a potential risk factor for oral cancer [64]. In a meta-analysis, the patient cohort of oral squamous cell carcinoma was associated with severe deficiency of vitamin D (mean serum level 12.2 ng/mL) [65]. Of relevance, the antineoplastic activity of 1,25(OH)₂D was shown in a wide variety of malignancies including oral squamous cell carcinoma [66].

4. Benefits of higher vitamin D status on oral health

It is an accepted fact that moderate exposure to sunlight is sufficient to maintain adequate level of vitamin D in the body to protect bones from diseases like rickets and/or osteomalasia [6,67]. Experts believe that approximately 5–30 min of exposure to sunlight between 10am to 3pm populated latitudes, at least twice a week, to the face, arms, legs, or back without sunscreen can provide with the required amount of vitamin D to most humans

Table 2
A few factors that influence vitamin D absorption from the sunlight [23,54].

- Aging
- Air quality (e.g., pollution)
- Application of sunscreen
- Location (e.g., higher latitude geographically)
- Lotions and creams
- Skin pigmentation
- Thicker epidermal layer

[38]. Of relevance, numerous factors may influence vitamin D synthesis, and a few are listed in Table 2.

In cross-sectional studies, low vitamin D level in the body has been associated with increased gingival inflammation, tooth loss, and maternal periodontal diseases during pregnancy [68]; calcium and vitamin D supplementation claimed to have reduced the severity of periodontal diseases, in a longitudinal study [69,70]. Similarly, conventional therapies with vitamin D analogs and phosphate supplements have a considerable beneficial impact on oral health in children with hypophosphatemic rickets [71]. Vitamin D can stimulate the production of cathelicidin and defensins that have antimicrobial properties, and thereby can help in reducing the number of bacteria in the oral cavity [72]. From the mid-1800s through the 1980s, solar UVB was inversely correlated with dental caries and tooth loss among adolescents and young men [73].

A direct role of sunlight in reducing the risk of periodontal diseases is shown in a Norwegian study, where a close relationship between tooth loss and latitude has been found.; For instance only 11% of people living in the south lost teeth compared to 43% living in the central region and 66% in the northern region [74–76]. A study in Brazil found that people with dark skin had a 50%–60% greater risk of periodontal diseases than people with light skin, perhaps related to difference in vitamin D synthesizing abilities [77]. In a similar line of observation in a US study, African-Americans were found to have a greater risk of periodontal diseases than White Americans. Of clinical relevance, African-Americans had average vitamin D blood levels of about 16 ng/mL (40 nmol/L) compared to 26 ng/mL (65 nmol/L) to white Americans; vitamin D is obtained from solar UVB exposure reaches less in the lower layer of dark skin, where vitamin D is produced.

In a study performed on the oral squamous cell carcinoma cell lines, Sundaram et al. demonstrated that 1,25(OH)₂D treatment resulted in inhibition of proliferation of tumor cell lines [78]. The authors speculated that vitamin D analogues might be used as therapeutic agents for limiting the growth of oral squamous cell carcinoma-type tumors [78]. In a similar line of study, mice fed with diet low in vitamin D resulted in unregulated cell proliferation, a hallmark of development of oral cancer [79]. Summarizing the above cited evidences, it is clear that higher vitamin D status has more beneficial effects on oral health, and exposure to safe sunlight can reduce the risk of periodontal diseases.

5. Conclusion

Maintaining disease free healthy oral function is important. As a bidirectional association between periodontal diseases and various systemic diseases are noted in type 2 diabetes mellitus [80], preterm low-birth weight infant [81], and cardiovascular diseases [82]. Such bidirectional association might be related to low vitamin D activities, In fact, low vitamin D status is proposed to be the link between chronic periodontitis and erectile dysfunction [83]. Periodontal diseases are usually associated with alveolar bone loss, possibly induced by the host immune response following bacterial insult. As mentioned, vitamin D exerts a vital role in bone

growth, proper function and its maintenance, as well as increases immunity (Fig. 1). There is a biological basis to suspect that an inadequate vitamin D status could adversely affect the periodontal health and oral functions, in general. In fact, low vitamin D level has been shown to be associated with increased gingival inflammation, tooth loss, clinical attachment loss, and higher rate of maternal periodontal illness during pregnancy [68,81]. Moreover, inadequate vitamin D status can compromise osseous healing in the oral cavity and beyond [84]. Growing awareness by dental health care providers for keeping the optimal vitamin D status is necessary for maintaining disease-free oral health is of the vital importance. As primary source of vitamin D is sunlight exposure, further studies are required to establish the fact that safe sunlight exposure for maintaining essential oral functions is extremely beneficial. Hypovitaminosis D usually reflects reduced or lack of sunlight exposure and humans have the innate ability to produce endogenous vitamin D following sunlight exposure. Since vitamin D deficiency is highly prevalent, attaining optimal vitamin D level is essential for maintaining oral health and beyond. As such, when available, safe sunlight exposure should be encouraged to have healthy oral and general health.

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