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Review Article

A Review of Exploring the Effects of Vitamin D Deficiency on Oral Health and Facial Structures

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ABSTRACT

Vitamin D, a steroid hormone primarily acquired through diet, supplements, and sunlight exposure, is crucial for maintaining calcium phosphate balance and bone turnover, thus supporting the musculoskeletal system. In addition, it plays an important role in the immune system's function. This review aimed to investigate the effects of vitamin D deficiency on the oral cavity, jaw, and facial structures. A comprehensive search was conducted on studies published in English from 2010 to 2024 across Google Scholar, Scopus, PubMed, and Medline databases. After reviewing various articles discussing the role of vitamin D in the body, particularly in oral and dental health, the impact of deficiency on disease development, and the potential benefits of supplementation in recovery, the findings highlight vitamin D's significant contribution to oral and dental health as well as immune system function. However, there were discrepancies regarding the effect of vitamin D on external root resorption in conditions such as Sjogren's syndrome and orthodontics, indicating a need for further clinical trials to validate these observations.

Keywords: Steroid hormones, Vitamin D, Oral health, Dental health

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Introduction

Throughout an individual's life, nutrition significantly influences overall health, including the condition and function of the teeth and oral structures. A well-balanced diet is crucial in maintaining this health. Malnutrition occurs when the diet fails to supply the necessary minerals, vitamins, and other nutrients required for the proper functioning of body tissues. Additionally, certain medications can contribute to nutritional deficiencies [1, 2]. Vitamins are essential organic compounds that function as catalysts in metabolic processes, antioxidants, transcription factors, and electron donors. Currently, 13 vitamins have been identified, with recommended minimum levels established to prevent deficiencies [3, 4].

Between these, vitamin D is particularly important as it helps regulate calcium and phosphate balance, which is essential for musculoskeletal health. Moreover, this vitamin is extremely important in the immune system's function [5, 6]. Vitamin D deficiency is widespread, with nearly 40% of individuals in Europe experiencing insufficient levels, and 13% suffering from severe

deficiency. While vitamin D can be obtained through dietary supplements or synthesized in the skin upon exposure to sunlight, factors such as environment and individual characteristics often limit the body's ability to produce adequate amounts [7].

In addition to its role in regulating calcium metabolism, vitamin D exhibits anti-cancer, anti-inflammatory, and anti-bacterial properties. These effects are crucial for maintaining the health of oral tissues, including the mucosa, bones, teeth, and periodontium [8, 9]. Despite its importance, the impact of vitamin D on oral health has not been extensively studied, warranting further investigation. This review aims to explore the role of vitamin D in the body, particularly within the context of dentistry, and the consequences of its deficiency on oral and dental health.

Materials and Methods

For this review, a comprehensive search was conducted for articles published in English between 2010 and 2024 across multiple databases, including Scopus, Medline, Google Scholar, and PubMed. The search utilized keywords such as "vitamin D deficiency," "vitamin D," "oral manifestations," "teeth," and "medical dentistry."

Studies were selected based on their relevance and quality, with those lacking sufficient or relevant data being excluded. Only studies that fulfilled the inclusion criteria, focusing on the role of vitamin D in dentistry and its impact on oral health, were incorporated into the review.

Results and Discussion

Vitamin D structure and its receptor

Vitamin D is a steroid hormone primarily derived from dietary sources, supplements, and sunlight exposure. There are two main forms of vitamin D: vitamin D3 (cholecalciferol), which is produced in the skin upon sunlight exposure, and vitamin D2 (ergocalciferol), which is obtained through food sources. The activation of this vitamin can also occur within oral tissues. Deficiency in vitamin D is defined by levels below 25 nmol/L. Common systemic consequences of vitamin D deficiency include osteomalacia in adults and rickets in children [5]. Several factors contribute to vitamin D deficiency, such as premature birth, being female, genetic predisposition, advanced age, obesity, malabsorption, darker skin pigmentation, and urban living [10].

Vitamin D exerts its effects through both genomic and non-genomic mechanisms. The genomic action is mediated by the vitamin D receptor (VDR), which is part of the nuclear receptor subfamily.

Figure 1 shows the schematic model for VDR (vitamin D receptor) regulation.

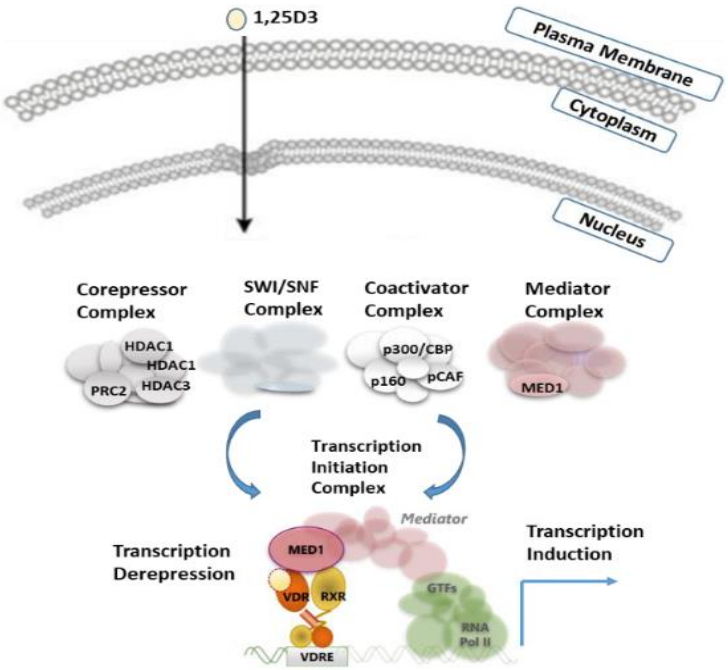

Figure 1. Schematic model for VDR (vitamin D receptor) regulation.

Vitamin D receptors are essential for maintaining the integrity and functionality of the skeletal system and can be found in various tissues such as bones, parotid glands, skin, kidneys, brain, and immune cells.

Variations in certain alleles of the vitamin D receptor (VDR) gene can influence vitamin D's cellular activity. VDRs play a role in several critical functions, including anti-inflammatory and anti-fibrotic responses, regulation of calcium metabolism, and the prevention of conditions like diabetic nephropathy, reduction of proteinuria, regulation of blood pressure, and protection against atherosclerosis [11].

Beyond genomic actions, vitamin D also exerts non-genomic effects through receptors that differ from the nuclear VDR. These include the activation of cellular kinases and proteases, as well as the release of prostaglandins. This process activates several cell types, including monocytes, enterocytes, chondrocytes, muscle cells, vascular smooth muscle cells, and osteoblasts [12].

The role of vitamin D in dentistry and the impact of its deficiency on oral health are visually summarized in **Figure 2**.

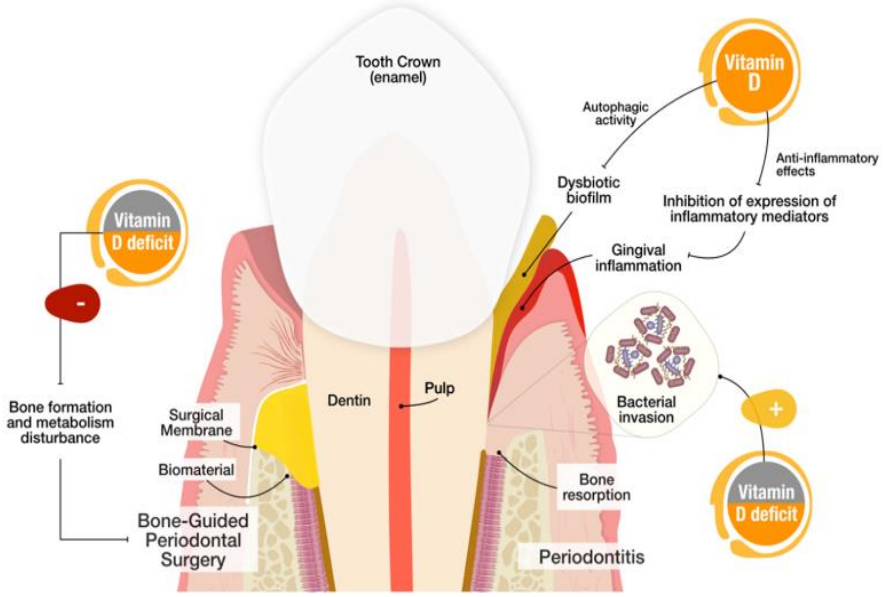

Figure 2. Vitamin D's role in dentistry and the effects of its deficiency in oral diseases.

Vitamin D and pediatric dentistry

Tooth decay

A deficiency in vitamin D can heighten the risk of cavities by interfering with calcium regulation and the process of tooth mineralization [13]. This essential nutrient plays a crucial role in the development of both the enamel and dentin, as well as in bone formation, with odontoblasts and ameloblasts being its primary target cells. When vitamin D is deficient during tooth development, it can lead to structural defects, such as enamel hypoplasia, which significantly increases the risk of severe early childhood caries (ECC). Additionally, factors such as low vitamin D and calcium levels, neonatal hypoxia, and gestational diabetes are contributing causes of enamel defects in primary teeth [14]. The vitamin D status of both the mother and child, as well as the improvement of vitamin D levels in expectant mothers, can influence the occurrence of ECC in infants [15, 16].

Tooth development

In children, tooth eruption delays are commonly caused by nutritional deficiencies, systemic health issues, hormonal imbalances, or syndromes, which can result in conditions like persistent primary teeth (PPT) and delayed tooth eruption (DTE). A study involving Brazilian children found that those with PPT had lower vitamin D levels, while vitamin D deficiency was linked to an increased occurrence of DTE. This underscores the importance of proper vitamin D levels in both mothers and infants for healthy tooth development. Low vitamin D concentrations during mid-pregnancy or at birth have been associated with delayed eruption of primary teeth [17].

Vitamin D in orthodontics

Several studies have explored the relationship between orthodontics and vitamin D. Clinical factors, along with variations in the vitamin D receptor gene, have been shown to influence external root resorption in orthodontic patients. In a study by Khalaf, the rate of tooth movement in orthodontic procedures was unaffected by vitamin D deficiency in rats [17]. Azizi's research also found no significant correlation between vitamin D levels and root resorption [18]. However, in Al-Attar's study, it was suggested that maintaining

adequate vitamin D3 levels could shorten orthodontic treatment time and reduce pain. Additionally, vitamin D supplementation increased bone mineral density, which led to slower tooth movement and less relapse in treatment outcomes [19, 20].

Vitamin D and the periodontium

Vitamin D is vital for preserving periodontal health. Its active form, 1,25-(OH)2D3, plays a significant role in gene regulation through the hydroxylase enzyme, promoting the production of proteins essential for cell adhesion and intercellular communication in epithelial cells. This enhances the strength of the physical barriers formed by these cells. Furthermore, vitamin D stimulates the production of antimicrobial peptides, which contribute to the body's innate immune response, potentially neutralizing bacterial components and providing defense against periodontal pathogens [21].

Vitamin D significantly contributes to the production of antimicrobial peptides, for example, cathelicidin and defensins, which defend the body against oral pathogens. These effects are mediated through the vitamin D receptor (VDR), which is essential for regulating genes that govern the production of cathelicidin hCAP-18 [22]. Studies have demonstrated that 1,25-(OH)2D3 encourages the differentiation of monocytes into macrophages, enhancing their phagocytic activity and lysosomal enzyme function. Also, this form of vitamin D inhibits the release of proinflammatory cytokines like IL-1, IL-6, and TNF-α. Furthermore, it increases the chemotactic and phagocytic abilities of macrophages. This enhancement helps mitigate alveolar bone loss and reduce inflammation in the gums. Variations in the VDR gene are also associated with conditions such as periodontitis, tooth loss, and bone degradation. Supplementing calcium and vitamin D has been shown to inhibit alveolar bone loss, enhance bone density in the jaw, and improve overall periodontal health. Patients in the maintenance phase of periodontal therapy who consume these supplements exhibit significantly better oral health compared to those who do not. These improvements were also observed in radiographic evaluations, where treatment with 1,25-(OH)2D3 facilitated the differentiation of human periodontal ligament stem cells into osteoblasts [23].

The process of osseointegration in dental implants is reliant on the body's ability to regenerate bone. Vitamin D deficiency can hinder this process and may contribute to early implant failure in some individuals [24]. Maintaining an adequate level of vitamin D is critical for the success of osseointegration, supporting both bone regeneration and the continued formation of bone around the implant post-loading. Several studies have shown a direct correlation between elevated serum vitamin D levels and the presence of osteoclasts around grafts used in bone augmentation. Furthermore, combining vitamin D with xenografts has shown positive effects on bone growth, bone shape, and implant stability [25]. Patients who were supplemented with vitamin D displayed higher peri-implant bone levels, confirming the vitamin's beneficial impact on implant success [26]. Garg P's research highlighted that patients who were vitamin D deficient and later received supplementation exhibited a significant improvement in marginal bone levels compared to those who did not receive supplements [26].

Despite these positive findings, there remains some debate about the role of vitamin D in implant osseointegration. According to a review by Alsulaimani, no clear causal relationship between low vitamin D levels and early implant failure has been established. However, it is suggested that vitamin D levels play a crucial role in osseointegration success, likely through its effects on immune system regulation and the healing process [27, 28]. A systematic review suggested that serum vitamin D levels may be linked to osseointegration, marginal bone loss, and the longevity of implants. It was recommended that patients' vitamin D levels be assessed before implant placement and supplemented if needed, though more clinical trials are necessary to confirm these findings [29]. Additionally, vitamin D may help reduce the risk of peri-implant infections and peri-implantitis, with a marked difference in serum 25(OH)D levels observed between those receiving and those not receiving vitamin D supplementation [30].

Vitamin D and bone and joint diseases

Medication-related osteonecrosis of the jaw (MRONJ) refers to the loss of the underlying bone in the jaw due to necrosis, a severe complication often associated with treatments like bisphosphonates, antiangiogenics, and denosumab, that are prescribed for certain cancers and osteoporosis. Vitamin D may play a key role in bone healing for patients suffering from osteonecrosis linked to bisphosphonates. As MRONJ can develop during any oral surgery, its risk can be mitigated through proper patient history, consultation with healthcare professionals, and the use of minimally invasive techniques like lasers. Research has highlighted that not only vitamin D but also parathyroid hormone (PTH) levels significantly influence the risk of developing osteonecrosis of the jaw, with vitamin D deficiency contributing to PTH and calcium

imbalances [31]. Supplementing with vitamin D may help protect against diseases that require bisphosphonate therapy, which increases the risk of osteonecrosis, thus acting as a preventive measure in high-risk cases [32].

Vitamin D and temporomandibular joint disorders

Several studies have explored the relationship between vitamin D deficiency and temporomandibular joint (TMJ) disorders, revealing that a lack of vitamin D can lead to increased pain and affect patients' daily activities [33, 34]. In a study by Demir, there were no significant differences in vitamin D levels between patients with TMJ disorders and healthy individuals. However, TMJ disorder patients exhibited elevated levels of parathyroid hormone because of vitamin D deficiency, suggesting that monitoring and correcting vitamin D deficiency in TMJ disorder patients is crucial [35, 36]. A systematic review also indicated that TMJ disorder patients typically have lower vitamin D levels, and variations in the vitamin D receptor (VDR) gene may be important in the development and progression of the condition. Although the exact mechanisms remain unclear, further research is needed to fully understand these relationships [34].

Vitamin D and oral cancer

Vitamin D has been shown to play a significant role in cancer prevention due to its various cellular effects, including anti-apoptotic, anti-inflammatory, anti-angiogenic, anti-invasive, anti-metastatic, and anti-proliferative properties. The active form of vitamin D carries out these actions by binding to the nuclear vitamin D receptor (VDR) in tissues, and since many tumors express VDR, this receptor could influence the development of cancer [35]. Oral supplementation of vitamin D has been found to enhance the effectiveness of photodynamic therapy in treating squamous cell carcinoma in mice, suggesting that vitamin D could serve as a valuable, non-toxic adjunct in cancer therapy. Laboratory studies have demonstrated that vitamin D increases the expression of VDR proteins and genes in various cell types. Yuan’s study further supported the role of vitamin D signaling in the pathophysiology of oral keratinocytes, both in vitro and in vivo. However, vitamin D deficiency alone is not sufficient to initiate carcinogenesis or disrupt oral epithelial homeostasis. Afzal's research revealed that low plasma vitamin D levels were associated with a higher risk of smoking-related cancers, such as squamous cell carcinoma of the head and neck. It is important to recognize that not all VDR gene polymorphisms are linked to cancer; the relevance of each polymorphism depends on the type of cancer. Additionally, it is essential to assess how VDR interactions with environmental factors, including diet and lifestyle, may influence cancer risk [36]. Sundaram’s study demonstrated that vitamin D inhibits the growth of various oral squamous cell carcinoma (OSCC) tumor-derived cell lines [37]. Vitamin D's regulatory effects on cytochrome P450 expression and its ability to inhibit OSCC cell proliferation suggest that vitamin D analogs could be potential therapeutic agents for managing OSCC progression.

Discussion

The serum levels of vitamin D in individuals with Recurrent Aphthous Stomatitis were notably lower compared to healthy controls, though it remains unclear whether this deficiency is a consequence or cause of the condition [35, 37]. Despite the absence of significant adverse effects from treatments or supplementation, the suggestion to use vitamin D as a treatment remains contentious [36]. Research by Nemati *et al*. [38] indicated that vitamin D deficiency plays a crucial role in the immune response in PFAPA syndrome, a condition where canker sores appear alongside febrile episodes of pharyngitis and cervical lymphadenopathy. In this study, patients with PFAPA had significantly lower vitamin D levels than the control group.

Studies investigating the relationship between vitamin D levels and the progression of Sjogren's syndrome have yielded mixed results. Bang and Muller found a negative correlation between vitamin D serum levels, the severity of clinical symptoms, and the concentration of inflammatory markers in the early stages of Sjogren's syndrome. In contrast, Baldini and Szodoray did not observe a reduction in vitamin D levels in cases of primary Sjogren's syndrome [39].

There is a notable link between vitamin D deficiency and oral candidiasis. Insufficient vitamin D results in elevated calprotectin levels in the blood, diminished neutrophil function, and an increased risk of opportunistic infections [40]. In AIDS patients, vitamin D deficiency contributes to a higher incidence of oral candidiasis, especially in individuals with CD4 lymphocyte counts below 200, with this deficiency acting as an environmental factor that exacerbates the condition [40].

Oral lichen planus (OLP), a chronic mucosal disease characterized by cycles of exacerbation and remission, may benefit from vitamin D's anti-inflammatory and immune-regulatory effects, as well as its role in regulating keratinocyte proliferation and differentiation. A systematic review revealed that all

studies included showed notable improvements in OLP symptoms when vitamin D supplementation was used alongside conventional steroid treatment or a placebo. However, further research with larger sample sizes is necessary to confirm these findings [41].

Vitamin D and the oral microbiome

Various oral diseases, including caries and periodontal disease, are linked to disruptions in homeostasis. The host immune system produces antimicrobial peptides (AMPs) that play a critical role in controlling the oral microbiome, preserving oral health, and preventing disease development [42, 43]. Additionally, dental mesenchymal stem cells might contribute to antibacterial defense by generating AMPs, absorbing phagocytic immune cells, and modulating their activity. These functions are amplified in inflammatory environments and are influenced by vitamin D levels.

Conclusion

This study has highlighted the critical role of vitamin D across various aspects of dentistry, emphasizing its significant impact on oral and dental health. Given the widespread prevalence of vitamin D deficiency, it is essential to understand its functions and ensure an adequate intake. Research suggests that the biological activation of vitamin D can also occur in oral tissues [44].

Vitamin D's importance begins early in fetal development, where maternal deficiency is linked to an increased risk of dental caries and impaired dental growth in the infant. Deficiency is particularly common during the 2nd and 3rd trimesters of pregnancy, making awareness programs on the importance of vitamin D during this period crucial. Additionally, vitamin D plays a role in orthodontic tooth movement, though studies show mixed results regarding its influence on root analysis [27, 29]. It also offers protection against periodontal diseases by preserving bone health and exerting anti-inflammatory and antibacterial effects [31]. Vitamin D’s influence on bone health may aid in alleviating TMJ joint pain and supporting bone repair in conditions like osteonecrosis, although further research is needed in this area [45, 46]. While vitamin D deficiency has been observed in patients with oral cancers, research by Yuan suggests that it alone is not sufficient to cause cancer. There is also debate surrounding vitamin D levels in patients with Sjögren's syndrome, as its serum concentration does not appear to be a definitive marker for the disease [47]. In cases of oral candidiasis, a link to vitamin D deficiency exists, though it does not seem to influence denture stomatitis, being more associated with candidiasis. Vitamin D supplementation has shown beneficial effects in managing oral lichen planus [48]. When vitamin D deficiency is caused by systemic conditions such as rickets, kidney diseases, or inflammatory bowel disease (IBD), oral manifestations on bones and teeth may occur.

A key role of vitamin D in the body is strengthening the immune system by promoting the production of antimicrobial peptides to combat opportunistic infections. Insufficient vitamin D levels can increase the risk of various respiratory infections, including COVID-19 [49].

In conclusion, vitamin D is essential not only for general health but also for maintaining oral and dental well-being. Its deficiency can lead to significant health issues, particularly concerning oral health. It is therefore recommended that public health programs include strategies to ensure adequate vitamin D levels within communities.

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