REVIEW ARTICLE

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Oral manifestations of vitamin D deficiency and potential treatment – Literature Review

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Abstract

Introduction and Objective. Vitamin D is essential for overall health, and particularly of the musculoskeletal system, including teeth. Its deficiency is linked to many oral health issues, such as caries susceptibility, impaired odontogenesis, delayed teeth eruption, implant failure and periodontitis. This review aims to examine the current knowledge of these effects and provide potential preventive and therapeutic effects of vitamin D supplementation.

Review Methods. The review is based on a search of recent literature from PubMed, Clinicaltrials.gov, and Google Scholar, consisting solely of English-language papers addressing the topic. All cited articles are less than eight years old.

Brief description of the state of knowledge. Vitamin D deficiency is associated with caries development due to its role in calcium and phosphate homeostasis, leading to teeth hypomineralization. The vitamin regulates odontoblast-like cells differentiation and OPG/RANKL activity. By influencing bone re-modelling, it determines the rate of teeth eruption. Some studies link its deficiency to teeth impaction. Additionally, vitamin D modulates the immune system, affecting osseointegration in implants and the progression of bone resorption in periodontitis. Nevertheless, more research is needed to understand the complex and often multifaceted mechanisms behind its impact on oral health.

Summary. Vitamin D plays a crucial role in oral health, though it is not a standalone remedy. It may serve as a safe, affordable adjunct to standard therapies. Further research could lead to more targeted interventions, especially for patients unresponsive to treatment. Early detection of vitamin D deficiency by healthcare providers can lead to improved diagnosis and better patient management.

Key words

vitamin D deficiency, oral health, dental caries, periodontal disease, tooth abnormalities, dental enamel hypoplasia

INTRODUCTION

Vitamin D is a fat-soluble vitamin primarily obtained in the skin from exposure to UVB light (290–315 nm) within the sunlight spectrum from 7-dehydrocholesterol, and can also be acquired from the diet (especially oily fish) or supplements [1]. Currently, vitamin D is considered a hormone due to its activation in the liver and kidneys, as well as its association with different systems of the body, including immune system function and calcium-phosphate metabolism [2]. The role of Vitamin D in the body is still the subject of research. Its main function is the regulation of intestinal calcium and phosphate absorption, providing optimal bone mineralization and serum calcium levels within the normal range [3]. Its non-calcaemic effects are also significant, as this receptor can be found in almost all tissue, including adipose tissue, brain cells and pancreatic beta-cells [4].

A lack of vitamin D can also be connected to many oral health issues, including dental mineralization defects [5,6], caries susceptibility[7], impaired odontogenesis [8], delayed teeth eruption [9], implant failure [10], prolonged wound healing [11] and periodontitis [12]. Vitamin D's actions can be categorized into genomic and non-genomic effects. Its cellular receptor (VDR) functions as a ligand-activated transcription factor, contributing to changes in gene expression, while non-genomic actions occur when the VDR is located outside the nucleus [13]. Measurement of serum 25-hydroxyvitamin D (25[OH]D) is a reliable marker to assess vitamin D status and blood concentration levels. Expert committees agree that a serum 25-hydroxyvitamin D [25(OH)D] concentration ≥50 nmol/L is generally considered adequate for bone and overall health in most adults[14].

To ensure consistency in interpreting experimental and clinical data, it is useful to provide a brief overview of how vitamin D dosages and concentrations are expressed

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and converted. Vitamin D_3 (cholecalciferol) is commonly reported in several units, including International Units (IU), micrograms (μg), mass concentrations (ng/mL), molar concentrations (nmol/L). By definition, 1 IU of vitamin D_3 equals 0.025 micrograms (μg) or 25 ng. Given its molecular weight (384.65 g/mol), 1,000 IU corresponds to 2,5000 ng, or approximately 65 nmol/L when dissolved in 1 litre of solution. Clinically, serum vitamin D levels are typically measured in nanograms per millilitre (ng/mL). To convert between these units and molar concentrations, a simple factor can be used: 1 ng/mL = 2.5 nmol/L. For example, a level of 20 ng/mL corresponds to 50 nmol/L. Percentage concentrations, such as 0.001%, refer to the mass of vitamin D per 100 mL of solution and can be converted to molar units using the molecular weight and volume.

OBJECTIVE AND REVIEW METHODS

The aim of this review is to examine the current understanding of the correlation between vitamin D deficiency and the development of oral health issues. As a result, potential preventive and therapeutic effects of vitamin D supplementation have been identified. However, the review also highlighted the need for more comprehensive and profound research. The review is based on an electronic database search of recent literature from PubMed, ClinicalTrials.gov, and Google Scholar. The key inclusion criteria, outlined at the beginning, were: only English-language papers addressing the topic, studies published within the last eight years, and the inclusion of meta-analyses and randomized clinical trials when available. In order to find the most recent publications, a search was carried out using key words: '25-hydroxycholecalciferol', 'vitamin D deficiency', 'vitamin D supplementation' in combination with terms related to oral health, such as 'periodontitis', 'tooth eruption', 'caries', and 'osseointegration', among others. Studies conducted on animals and those not written in English were excluded from this review at the beginning. Subsequently, the full texts of the relevant articles were retrieved and analyzed. Out of 452 studies independently collected by the co-authors, 180 were duplicates. An additional 105 studies were excluded due to poor quality or subjective concerns – for example, overly brief content, incoherent conclusions, or reliance on outdated data. This left 167 articles, from which 40 were selected as the most valuable and informative, based on journal limitations, relevance, and the potential significance of their findings. Among these 40 articles, there are 6 meta-analyses, 5 systematic reviews, and 29 original research papers, which include also randomized and cross-sectional studies.

DESCRIPTION OF THE CURRENT STATE OF KNOWLEDGE

Caries development. Numerous review papers and meta-analyses have examined the potential link between serum vitamin D levels and the risk of dental caries. This connection seems particularly plausible due to the effect of vitamin on the musculoskeletal system, of which the teeth are a part, as well as its role in calcium and phosphate metabolism.

A recent French meta-analysis [15] found a statistically significant association between low 25(OH)D levels and an increased risk of dental caries, compared to the higher levels. This effect appears to be particularly evident in children [7,15]. Supporting this, a Chinese meta-analysis published in 2020 found that low vitamin D serum levels increased the risk of caries in children by 11% [16] and varied across other groups. Similar results emerge from another paper [17] analyzing 13 studies published between 1998 – 2019.

Surprisingly, Nørrisgaard et al. found no statistically significant relationship between Vit. D3 supplementation (2800 IU/day vs. 400 IU/day placebo) and caries risk in both deciduous and permanent dentition during pregnancy. However, higher doses of vitamin D3 were associated with a 50% reduction in the odds of enamel defects in children at the age of 6 [18]. It is important to note that the placebo group in this study received a low dose of 400 IU/day of vitamin D rather than no supplementation. This approach reflects ethical considerations and current clinical guidelines, as vitamin D is essential for maternal and foetal health. Complete withholding of vitamin D could pose risks; therefore, 400 IU/day was administered as a minimal dose to maintain sufficiency while enabling assessment of the effects of higher doses on dental outcomes.

A 2023 study [7] found that children with vitamin D deficiency had a 22% higher risk of developing dental caries compared to those with adequate vitamin D levels. Additionally, when analyzed by age group, the results revealed on average a 28% higher risk in permanent teeth studies, a 68% higher risk in deciduous teeth studies, and an 8% higher risk in mixed dentition studies. Gyll et al. investigated the relationship between vitamin D levels in 6-year-old children and their caries status two years later. Initially, there seemed to be no significant difference in vitamin D levels between the groups. However, after adjusting for confounding factors at the multivariate level, the study found that lower 25(OH) D blood serum levels were independently associated with the presence of dentin caries in both types of dentition [19].

It is important to note that the certainty of the evidence, according to the GRADE approach, was rated as low. Age and family income were identified as key sources of heterogeneity in the results [15–17]. Cross-sectional studies were commonly used, which limited the ability to clearly establish causality. Although the included meta-analyses controlled for factors such as race, ethnicity, sugar intake, and gender, some variability in the results remained.

Effect of vitamin D on caries progression. Vitamin D plays a crucial role in regulating plasma calcium and phosphate levels during dentin development and supports mineralization by binding to dental cells. Its deficiency disrupts the complete fusion of calcospherites, resulting in the formation of less mineralized tissues. In this way, insufficient vitamin D concentration in the body serves as the primary biochemical factor contributing to the presence of incompletely mineralized areas in dentin [20]. These areas are more susceptible to severe damage from caries, as bacteria promote the demineralization of dentin which, due to already existing incomplete mineralization, is even more prone to decay.

An study in India [21] found that children with dental caries have reduced salivary calcium levels compared to those without caries, while their salivary phosphate levels were elevated. The study showed a link between vitamin D deficiency and lower salivary calcium levels. These results imply that both factors

may be potential risk factors for the development of caries. Acid-producing bacteria promote demineralization, but vitamin D helps maintain sufficient calcium and phosphate levels in saliva, promoting subsequent remineralization [21]. Furthermore, studies have shown that vitamin D regulates the immune system, leading to the production of anti-microbial proteins like defensins and proteases, which target cariogenic bacteria. An *in vitro* study found that both vitamin D2 and D3 exhibited antimicrobial properties against Streptococcus mutans, although the limitations of the study should be considered in interpreting the results [22].

Teeth mineralization defects and impaired odontogenesis. Scientists have been attempting for several years to investigate the link between vitamin D deficiency during foetal life and early pos-tnatal development, and the development of enamel and dentin defects. The research results are still unclear, but several researchers have made bold conclusions.

In healthy individuals, dentin is characterized by homogeneity and complete fusion of calcospherites; however, in cases of vitamin D deficiency, incomplete fusion of calcospherites results in a hypomineralized region within the matrix. Disruptions in the metabolic pathways involving vitamin D lead to systemic defects in mineralization, manifesting in teeth as inter-globular dentin (IGD) [5,20]. According to Veselka, IGD – which indicates vitamin D deficiency – can still be detected in cremated remains, enabling the assessment of vitamin D deficiency even in teeth exposed to high temperatures (over 900 °C).

Korun et al. [23] discovered a significant association between low umbilical cord 25(OH) D levels (<75 nmol/L) and enamel hypoplasia, which is a risk factor for caries expansion. They concluded that low umbilical cord 25(OH) D played a major role in early childhood caries development. The detection of vitamin D receptors (VDR) in ameloblasts and odontoblasts suggests that Vit. D3 plays a role in regulating enamel and dentin formation. This regulation disruption can result in enamel hypoplasia and hypophosphatemia, which in turn leads to the development of interglobular dentin [24].

In contrast, Dave concluded that although low levels of vitamin D may impact primary tooth development, the evidence supporting this link is rather limited [25]. Similarly, van der Tas et al. showed no associations of foetal, neonatal, and child vitamin D status with the presence of enamel hypomineralization [26].

Delayed eruption of teeth. Dhamo et al. found that insufficient vitamin D levels during the pregnancy and time of birth were linked to delayed eruption of primary teeth [27]. Crincoli et al. explored the connection between Vit. D deficiency and impacted mandibular third molars, discovering that 25(OH) D3 levels were lower in the patient group compared to the control group [28]. Sahin, in a study involving paediatric patients, suggested that low levels of 25(OH)D_3 and calcium, accompanied by elevated parathyroid hormone levels, could be linked to the delayed teeth eruption [29].

A consistent conclusion also arises from a study conducted on children by Xavier et al., suggesting that vitamin D deficiency may be a risk factor for delayed tooth eruption associated with persistent primary teeth [30].

Unfortunately, the amount of research and data on this subject is currently insufficient for an objective assessment.

Dental implant failure. A review by Sundar et al. [31] indicates that Vitamin D supports bone regeneration in bone defects and enhances osseointegration around implants. *In vitro* studies have shown that Vit. D stimulates osteogenic markers and increases the expression of genes of bone matrix proteins and alkaline phosphatase in osteoblasts [31]. While clinical evidence remains limited, the affordability and non-invasive nature of Vit. D make it a promising topic for further research.

Although vitamin D deficiency appears to negatively affect bone quality, implant failures did not consistently correlate with vitamin D deficiency alone – periodontitis, diabetes, and smoking may be considered as confounding factors [32]. Supporting literature presents mixed results: some studies report no significant relationship between Vit. D deficiency and early dental implant failure, while others suggest that low vitamin D levels may impair osseointegration, particularly in medically compromised individuals.

The results of two studies assessing the link between serum vitamin D levels and early dental implant failure did not demonstrate a statistically significant association. In the first study [33], which included 1,625 implants, 3.2% of early failures were reported. While failure rates appeared to increase with lower vitamin D levels, the differences were not statistically significant. In the second study [34] involving 174 implants, eight early failures occurred, yet the mean vitamin D level was actually higher in the failure group (42.54 ng/mL) than in the successful group (31.92 ng/mL). Findings suggest that, despite an observed trend, low vitamin D levels were not conclusively linked to early implant failure. The direct impact of vitamin D deficiency on dental implant integration has yet to be definitively established.

Periodontal disease. A meta-analysis conducted by Liang et al. [35] examined the impact of scaling and root planing combined with vitamin D supplementation on individuals with periodontitis. The results indicated that scaling and root planing + vitamin D significantly increased serum vitamin D levels compared to the treatment alone. Furthermore, a combination of scaling and root planing + vitamin D helped reduce clinical attachment loss, but it did not have a statistically significant effect on probing depth, gingival index, or bleeding index, possibly due to insufficient vitamin D dosage or treatment duration. The combination of scaling, root planing and vitamin D was shown to be more effective in clinical attachment loss reduction. Analysis also confirmed that individuals with periodontitis tend to have lower serum vitamin D levels compared to healthy individuals. Additionally, the meta-analysis revealed significant heterogeneity among the studies.

Laky et al. [36] state that low serum levels of 25(OH)D are significantly linked to periodontal disease. In cases of periodontitis, low vitamin D levels may impair this immune transition, potentially leading to a more abrupt progression of the inflammatory state and bone loss. Another study [37] confirmed that there was also a statistical reduction in *P. gingivalis*, *T. denticola*, and *T. forsythia* following vit. D oral administration for a 2-month period.

Potential preventive and therapeutic effects of vitamin D supplementation. The results of studies so far do not provide straightforward answers and are not impressive. A randomized clinical trial by Perić et al. [38] aimed to

evaluate the effect of vitamin D as the sole adjunct to non-surgical periodontal treatment. The supplementation of Vit. D 25,000 IU/ week for six months proved to be both safe and effective in elevating serum levels in periodontal patients receiving non-surgical treatment. Additionally, there was a trend toward a greater reduction in the depth of periodontal pockets ≥ 4 mm in the vitamin D-treated group. However, the study acknowledges the limitation of the small sample size. Unlike antibiotic-based trials, vitamin D may take more time to produce noticeable effects, meaning that follow-ups at three or six months should be interpreted with caution.

Another double-blinded clinical trial [39] involved 975 healthy infants under 2-years-old who received daily vitamin D3 supplementation (10 µg vs. 30 µg). In the follow-up study at 6 – 7 years, 123 children were examined to evaluate tooth enamel defects, caries progression and tooth eruption. Enamel defects were found in 39% of children in the 10 µg group and 53% in the 30 µg group. The majority of the children (94%) had adequate vitamin D levels, and 88% were free from caries. No significant correlations were observed between the vitamin D supplementation during infancy and oral health outcomes or the occurrence of enamel defects.

A cross-sectional study of 1,638 Polish children [40] examined the impact of vitamin D supplementation on oral health. The results showed that children who received vitamin D had lower prevalence of early childhood caries and severe ECC. However, after adjusting for other factors, supplementation was not significantly associated with caries, although decayed teeth remained linked.

Limitations of the study. Although this review highlights a growing interest in the role of vitamin D in oral health, several limitations should be considered. Many of the studies included were small, cross-sectional, or varied widely in design, making it difficult to draw clear conclusions. Definitions of vitamin D deficiency, dosage levels, and study outcomes varied across the literature, which limited comparability. The studies were conducted in various countries around the world, which also made it difficult to compare results due to regional differences in health care systems, diet and population characteristics.

Some important factors, e.g. diet, sun exposure, and overall health, were not always controlled, and the exclusion of older studies may have omitted relevant data. Lastly, most studies had short follow-up periods, and few explored long-term effects. More high-quality, consistent research is needed to better understand how vitamin D truly impacts oral health.

SUMMARY

The review highlights the role of vitamin D in oral health, emphasizing its contributions to calcium and phosphate metabolism, as well as the link between its deficiency and the development of oral diseases. While much is known about the skeletal benefits of vitamin D, its impact on oral health continues to emerge.

Despite promising links between Vit. D status and oral health, the evidence remains inconsistent. Many of the reviewed studies are characterized by small sample sizes and cross-sectional designs. Some studies suggest that vitamin D supplementation may reduce the risk of dental caries, enhance tooth mineralization, and improve periodontal health, but the overall impact remains uncertain. More rigorous clinical trials, including well-designed randomized controlled trials and meta-analyses, are needed to clarify the exact role of Vit. D in oral health and to define optimal supplementation strategies.

The potential therapeutic effects of vitamin D supplementation in preventing and managing oral health conditions are still an area of research. Current findings suggest that while vitamin D could be a valuable adjunct in oral health care, it should not be regarded as a panacea. A more comprehensive approach, including proper nutrition, oral hygiene, and lifestyle modifications, is essential for maintaining optimal oral health. Further high-quality research is necessary to refine our understanding of vitamin D's clinical significance, guide treatment protocols, and establish effective preventive strategies for both patients and practitioners.

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