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The effect of Vitamin D deficiency on the occurrence of enamel hypoplasia in babies: A review article

Salma Putri Widyanti [1,*], Emmanuel Andrew [1] and Tantiana [2]

[1] *Faculty of Dental Medicine, Airlangga University, Surabaya, Indonesia.*
[2] *Department of Oral Biology, Faculty of Dental Medicine, Airlangga University, Surabaya, Indonesia.*

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Abstract

Background: Vitamin D is a steroid prohormone that can be obtained primarily from exposure to sunlight and can also be obtained from food or supplements. Vitamin D has an important role in various metabolisms and developments in the human body, including in the process of odontogenesis or tooth development. Vitamin D deficiency can be associated with various problems in the oral cavity, in this case it has the potential to trigger enamel hypoplasia. Enamel hypoplasia is a quantitative defect in enamel, which appears as pits, grooves, missing enamel or smaller teeth. This literature study will discuss the relationship between Vitamin D concentration and dental development in early childhood.

Method: The method used is an article review that was conducted by analyzing various articles on related themes on virtual platforms such as PubMed, Google Scholar, ProQuest, and Science Direct.

Results: Vitamin D significantly affects the development of teeth in fetuses to babies.

Conclusion: Vitamin D plays an important role in various metabolisms and development of the human body. Vitamin D deficiency can cause developmental disorders and various diseases of the oral cavity such as enamel hypoplasia.

Keywords: Vitamin D; Deficiency; Odontogenesis; Hypoplastic enamel; Pregnancy; Babies

1. Introduction

Vitamin D is a steroid prohormone that is essential for human health, primarily sourced from sunlight and available in certain foods and supplements. Foods like oily fish, including salmon and mackerel, are natural sources. Vitamin D can be divided into two, namely Vitamin D2, derived from yeast through ultraviolet light and Vitamin D3, produced exposure to sunlight, namely through ultraviolet irradiation with 7-dehydrocholesterol from lanolin [1]. Active metabolites of Vitamin D such as 1,25-dihydroxy Vitamin D3 (1,25(OH)2D3) are crucial for bone metabolism, offering benefits for both physical and oral health [2]. Including the process of tooth development known as odontogenesis [3]. Adequate levels are considered above 50 nmol/L, with deficiency defined as below 25 nmol/L [4].

Vitamin D plays a pivotal role in the mineralization of bones and teeth, with insufficient levels leading to increased risks of fractures and decay due to hypomineralization [5]. Deficiencies can stem from both external (lack of sunlight or nutrition) and internal (genetic) factors, affecting both children and adults [6]. In children, the deficiency can lead to rickets, a condition marked by poor bone mineralization, while adults may experience osteomalacia. Additionally, maternal Vitamin D levels are crucial for prenatal health, influencing the risk of several conditions including gestational diabetes and low birth weight [4].

* Corresponding author: Salma Putri Widyanti

The impact of Vitamin D on fetal and postnatal growth is significant, particularly through its role in calcium absorption [7]. In children, severe Vitamin D deficiency characterized by a 25-hydroxy Vitamin D status of less than 10 ng/mL can lead to rickets, with symptoms including skeletal deformities and delayed growth. This condition can also affect dental health, contributing to enamel hypoplasia, a defect that increases susceptibility to dental caries [8].

Enamel hypoplasia results from inadequate mineralization during tooth development, leading to teeth with holes, grooves, or missing enamel [4]. This condition underscores the importance of Vitamin D in dental health, particularly during the stages of tooth development. Evidence suggests that enamel hypoplasia is a significant risk factor for early childhood caries, highlighting the need for further research into its prevention and the role of Vitamin D [7].

In response to the prevalence of Vitamin D deficiency and its implications, health recommendations include supplementing infants with 8-10 µg of Vitamin D daily up to the age of one, and 10 µg for children aged 1-4, especially if they have limited exposure to sunlight or are not consuming formula milk fortified with Vitamin D. These guidelines aim to mitigate the risk of deficiency and promote overall health, demonstrating the critical role of Vitamin D in human development and disease prevention[9].

2. Materials and methods

The method used in writing this review article is to search and analyze various articles and journals through various platforms such as Pubmed, Google Scholar, ProQuest and Science Direct using several keywords such as: "Vitamin D" AND "Human Tooth Development" OR "Odontogenesis " AND “Deficiency” AND “Enamel Hypoplasia” AND “Babies”. Reference lists of selected articles were manually searched for additional relevant publications that may have been missed in the database search (saturation). All original English-language articles and reviews were retrieved as full text, and bibliographies were manually cross-checked for additional relevant articles.

3. Results and discussion

Table 1 Randomized controlled trials effect of Vitamin D deficiency with various problems in the oral cavity.

Title & Author	Subject	Method	Results
Vitamin D Deficiency and Oral Health: A Comprehensive Review. João Botelho, Vanessa Machado, Luís Proença, Ana Sintra Delgado, and José João Mendes (2020) [10]	Patients with Vitamin D deficiency collected from several articles.	The method used is a comprehensive review by analyzing various articles.	There is a strong correlation between Vitamin D deficiency (VDD) and various oral health issues, including an increased risk of dental abnormalities, cavities, gum disease, and failures in oral treatments. Ensuring sufficient levels of 25(OH)D is crucial for dental development and maintaining good oral health throughout a person's life. However, further research is needed to conclusively determine the benefits of correcting VDD through supplements, which could inform future clinical recommendations.
Prenatal Vitamin D and Enamel Hypoplasia in Human Primary Maxillary Central Incisors: A Pilot Study. Susan G. Reed, Delia Voronca, Jeanette S.	170 pairs of expectant mothers and their children.	The approach adopted was a single-site, placebo-controlled, double-blind, randomized clinical study focusing on the effects of Vitamin D supplementation throughout pregnancy.	In the first 8 weeks of the study, data from 29 out of 37 children, averaging 3.6 years old with a standard deviation of 0.9, were analyzed. This group was comprised of 48% boys and had a racial composition of 45% White, 31% Hispanic, and 24% Black. Enamel hypoplasia (EH) was detected in 13 (45%) of these

Wingate, Mallika Murali, Andrew B. Lawson, Thomas C. Hulsey, Myla D. Ebeling, Bruce W. Hollis, and Carol L. Wagnera (2017) [6]			children. It was observed that the mean levels of maternal 25(OH)D were notably lower in children who were diagnosed with EH.
Oral Manifestations of Vitamin D Deficiency in Children. Andrew Fulton, Maya Amlani, Susan Parekh (2020) [4]	Children aged 7-10 years.	Using article review and case-report methods in several journals or research that has been conducted previously.	The rise in Vitamin D deficiency during infancy is becoming more prevalent, potentially impacting the development and future condition of permanent teeth. The deficiency can lead to enamel anomalies that manifest as distinct bands or affect the entirety of the teeth.
Toward Preventing Enamel Hypoplasia: Modeling Maternal and Neonatal Biomarkers of Human Calcium Homeostasis. Susan G Reed, Cameron S Miller, Carol L Wagner, Bruce W Hollis, Andrew B Lawson (2020) [11]	350 healthy women of African American, Caucasian, and Hispanic descent from Charleston, South Carolina (SC), with single pregnancies, along with their infants from birth up to the age of 5 years.	Applying Bayesian analysis to secondary data from a randomized trial on prenatal Vitamin D3 supplementation in healthy expectant mothers (N=350) and subsequent research on a child subset.	In children, the occurrence of enamel hypoplasia (EH) was found to be 41% (60 out of 145), primarily in the incisal and middle sections of teeth. After adjusting for maternal factors, levels of cord blood intact parathyroid hormone (iPTH) and 1,25-dihydroxyVitamin D (1,25(OH)2D) showed a significant correlation with EH prevalence. An increase of 1 pg/mL in iPTH levels in cord blood corresponded to a roughly 6% decrease in EH prevalence, whereas a 10 pg/mL rise in 1,25(OH)2D levels led to an almost 30% increase in EH prevalence.
Vitamin D Supplementation in Pregnancy and Lactation and Infant Growth. Daniel E Roth, Shaun K Morris, Stanley Zlotkin, Alison D Gernand, Tahmeed Ahmed, Shaila S Shanta, Eszter Papp, Jill Korsiak, Joy Shi, M Munirul Islam, Ishrat Jahan, Farhana K Keya, Andrew R Willan, Rosanna Weksberg, Minhazul Mohsin, Qazi S Rahman, Prakesh S Shah, Kellie E Murphy, Jennifer Stimec, Lisa G Pell, Huma Qamar,	Women in good health, who were between 17 and 24 weeks pregnant, participated in a study from March 2014 to September 2015 at the Maternal and Child Health Training Institute (MCHTI) in Dhaka, Bangladesh.	In a study conducted in Bangladesh, the impact of prenatal Vitamin D supplementation, administered weekly from 17 to 24 weeks of pregnancy until delivery, alongside postnatal Vitamin D supplementation, was evaluated using a randomized, double-blind, and placebo-controlled approach.	There were no significant variations in the average length-for-age z scores across the different groups. The scores for the placebo group were -0.93±1.05, for the prenatal 4200 IU group -1.11±1.12, for the group receiving 16,800 IU before delivery -0.97±0.97, for the prenatal 28,000 IU group -1.06±1.07, and for the group receiving both prenatal and postpartum 28,000 IU -0.94±1.00, with a P-value of 0.23 indicating no significant global differences among the groups. Similarly, there were no significant differences in other body measurements, birth outcomes, or health issues among the groups.

Abdullah Al Mahmud (2018) [7]			
Vitamin D supplementation for term breastfed infants to prevent Vitamin D deficiency and improve bone health. Tan, M. L., Abrams, S. A., & Osborn, D. A. (2020) [12]	In the studies reviewed, 2,837 pairs of mothers and their infants were involved. All infants were full-term, healthy, and were either single births. They joined the study at birth or within the first six weeks postpartum.	Includes randomized controlled trials (RCTs) or quasi-RCTs. Exclude cross-over studies.	Out of eleven studies, all but two indicated instances of Vitamin D deficiency or insufficiency among infants at the conclusion of the intervention or follow-up, reporting infants with 25-OH Vitamin D levels below 50 nmol/L.
High-dose Vitamin D supplementation in pregnancy reduces rates of enamel defects in children. Tester, A A& Capaldi, F. (2021) [13]	Conducted in Denmark at the Gentofte and Naestved Hospitals, this study involved 623 women and their 588 corresponding children who were recruited between March 2009 and November 2010.	This involved a post hoc secondary examination of individuals enrolled in the Copenhagen Prospective Studies on Asthma in Childhood 2010 (COPSAC) initiative. The study's methodology included blinding both the researchers and dental examiners to the allocation of treatments, with participant randomization achieved through computer-generated numbers.	Administering a high dosage of Vitamin D supplements during pregnancy has been found to decrease the occurrence of enamel defects in children.
Effects of early Vitamin D deficiency rickets on bone and dental health, growth and immunity. Zerofsky, M., Ryder, M., Bhatia, S., Stephensen, C.B., King, J., & Fung, E.B. (2016) [14]	All children identified with Vitamin D Deficiency (VDD) rickets at the Children's Hospital & Research Center Oakland (CHRCO) between 2000 and 2009 were extended an invitation to take part in the Bone Health Day at the Children's Hospital Oakland Research Institute (CHORI).	The methods for biochemical and immune function analysis, alongside techniques for assessing anthropometry and bone density, medical histories, and dental examinations are detailed in the Supplementary Information Appendix S1.	No significant differences were observed in the gender or age of children with rickets compared to their healthy counterparts at the time of the study.
Etiology Study of Acquired Developmental Defects of Enamel and Their Association with Dental Caries in Children between 3 and 19 Years Old from Dolj County, Romania. Popescu, M., Ionescu, M., Scrieciu, M., Popescu, SM, Mercuț, R., Amărăscu, MO,	This study extends earlier research from January-February 2020 involving 213 children aged 3-19 from Poiana Mare in the Dolj region of Romania, who were students at the "George Ștefan Marincu" High School.	This study is a cross-sectional statistical analysis that first determines the prevalence of Dental Developmental Defects (DDE) in children through clinical evaluations and then seeks to pinpoint risk factors associated with DDE by analyzing questionnaires filled out by their mothers.	The study found no statistically significant link between Dental Developmental Defects (DDE) and factors such as pregnancy progression, maternal health status, or the child's health during early years.

Iacov Crăiţoiu, MM, Lazăr, D., & Mercuţ, V. (2022) [15]			
Association between Vitamin D and Dental Caries in a Sample of Canadian and American Preschool-Aged Children. Williams, T.L., Boyle,J., Mittermuller, B.-A., Carrico, C., & Schroth, R.J. (2021) [16]	Children under the age of 72 months from two distinct regions in North America.	Data was gathered from two separate studies, including a case-control study focusing on children under 72 months and their parents or primary caregivers. This study examined the relationship between levels of 25-hydroxyVitamin D (25(OH)D) and severe early childhood caries (S-ECC).	Data were collected from 344 children, of which 144 did not have caries, while 200 were diagnosed with S-ECC. The average age of the participants was approximately 42.1 months, with a standard deviation of 14.6 months, indicating a fairly even distribution of ages among the children.
Vitamin D status and tooth enamel hypomineralization are not associated in 4-y-old children: An Odense Child Cohort study. Nicoline, BM, Dorte, H, Christine, D., Signe, MN, Lene, C., Emily, C., Asta, R., Soren, M., Henrik, TC (2022) [17]	2,876 women registered for the OCC in Odense, Denmark.	The research utilized data from the OCC, a cohort study that is observational and based on the general population.	There is no relationship between Vitamin D status during pregnancy and HSPM in children at the age of four years.
The Influence of Prenatal Vitamin D Supplementation on Dental Caries in Infants. Robert, JS, Jodie, C., Margaret, M., Patricia, G., Betty, AM, Cheryl, RG (2020) [18]	Expectant mothers from the Outpatient Department of the Women's Hospital at the Health Sciences Centre in Canada.	The participants were split into two categories: those who were given Vitamin D and those who were not. Following this, interviews were conducted with the participants, and the collected data was processed through analytical software.	A notable disparity exists in the count of decayed primary teeth among children of mothers who took Vitamin D compared to those whose mothers did not.

4. Discussion

Vitamin D, in collaboration with parathyroid hormone (PTH), fibroblast growth factor 23 (FGF23), and calcitonin, is pivotal in the regulation of calcium and phosphate metabolism, which are foundational for the growth and maintenance of the musculoskeletal framework. This regulation is vital for bone development and the maintenance of bone health, impacting both physical and dental well-being, particularly in the formation of teeth [2].

The body acquires Vitamin D from two main sources: endogenously, through the synthesis in the skin triggered by ultraviolet B (UVB) radiation from sunlight, and exogenously, from dietary intake. This nutrient's active forms, especially 1,25-dihydroxy Vitamin D3 (1,25(OH)2D3), play a significant role in bone metabolism, promoting numerous health benefits that are crucial during the odontogenesis process, the development of teeth [2].

Vitamin D's role extends to the regulation of mineral homeostasis, influencing the intestinal absorption, renal reabsorption of calcium and phosphorus, and the mobilization and deposition of calcium in mineralized tissues [10].

Insufficiency in Vitamin D leads to hypocalcified dentin and delayed tooth eruption; thus, indicating that Vitamin D has an important role in dentin formation. Form active Vitamin D, 1α,25-dihydroxy Vitamin D3 (1α,25(OH)2D3), plays an important role in regulating bone and mineral metabolismalization of bone and tooth tissue [3].

The optimum concentration of Vitamin D in serum should exceed 50 nmol/L, with levels falling below 25 nmol/L categorized as deficient [4]. This deficiency can lead to hypomineralization, which compromises the integrity of bone and tooth, elevating the risk of fractures and dental decay [5]. Vitamin D deficiency can be attributed to both external factors, such as insufficient sunlight exposure or dietary intake, and internal factors, including genetic disorders affecting Vitamin D metabolism [6].

According to Zerofsky, et al [14, 19], Vitamin D deficiency in children can manifest as rickets, a condition marked by inadequate bone mineralization, increasing their susceptibility to fractures, asthma, and dental enamel damage. This indicates the broader implications of Vitamin D on health, suggesting that deficiencies in early life could potentially increase disease risk in later years.

Moreover, rickets is associated with dental anomalies, including enamel hypoplasia, a condition that makes teeth more vulnerable to caries [1]. Enamel hypoplasia, characterized by localized deficiencies in enamel, can be identified by various defects such as pits or grooves [4]. The development of enamel, which begins in utero and concludes before tooth eruption, can be significantly affected by maternal Vitamin D levels, emphasizing the nutrient's importance from prenatal stages through childhood [6].

Studies have highlighted the relationship between maternal Vitamin D levels during pregnancy and the incidence of enamel hypoplasia in children, showing a correlation between higher maternal Vitamin D concentrations and reduced enamel defect risks [7]. According to research conducted by Reed et al [11], the levels of umbilical cord blood iPTH and 1,25(OH)2D significantly associated with EH level after controlling for maternal factors. For every 1 pg/mL increase in cord blood iPTH, EH levels decrease by approximately 6%, whereas with each 10 pg/mL increase in cord blood 1,25(OH)2D, EH levels increase by almost 30%. These findings underscore the impact of prenatal nutrition on dental health, further supported by research indicating that prenatal calcium antacid usage could mitigate the severity of enamel hypoplasia.

This is also supported by research conducted by Reed et al [6], indicates a potential link between enamel hypoplasia (EH) in primary maxillary central incisors of children aged 2-5 and lower maternal serum 25(OH)D levels during pregnancy. The study observed EH prevalence across different treatment groups, with hypoplasia identifiable as early as 12 weeks into gestation and influenced by various supplementation factors. Longitudinal analysis revealed that women with serum 25(OH)D concentrations below 15 ng/ml during pregnancy (16-40 weeks) had a higher incidence of EH in their offspring (50%, 2 out of 4) compared to those with levels at or above 32 ng/ml (44%, 7 out of 16), although this difference was not statistically significant (Fisher's test p value = 1). The findings suggest that children born to mothers with lower Vitamin D levels (<15 ng/ml) during pregnancy have a higher relative risk of developing EH, underscoring the importance of adequate maternal Vitamin D levels for reducing the risk of EH in children.

It's crucial to acknowledge that there are multiple causes for hypoplastic teeth, and the diagnosis of chronic hypoplasia linked to Vitamin D deficiency is specifically made for individuals identified with Vitamin D deficiency, or those who experienced delayed walking or leg bending in infancy [8]. The relationship between Vitamin D deficiency and molar incisor hypomineralization (MIH) remains unclear, with studies showing mixed results. One research indicated that higher levels of Vitamin D were associated with a lower occurrence of MIH, whereas another investigation, which looked at Vitamin D levels during fetal, neonatal, and childhood periods, found no significant association with MIH[4].

Furthermore, low levels of Vitamin D have been identified as a factor increasing the likelihood of cavities in children. Those suffering from Severe Early Childhood Caries (S-ECC) exhibited considerably lower levels of 25(OH)D compared to their caries-free counterparts ($p < 0.001$). Additionally, children with insufficient 25(OH)D levels were found to be at a tenfold greater risk of developing S-ECC ($p < 0.001$) [16].

Given the significant impact of Vitamin D deficiency, particularly in infants, there are preventive measures that can be implemented. The National Health Service (NHS) advises a daily Vitamin D supplement of 8–10 μg for infants under one year old (except those who consume formula milk enriched with Vitamin D), and a 10 μg supplement for children between 1–4 years old. It's also suggested that infants should either spend less time outdoors or be adequately covered with clothing to protect their skin [9].

Current evidence is not strong enough to support the routine supplementation of Vitamin D for breastfeeding mothers

or infants in groups with a lower risk of deficiency [7]. However, for populations at a greater risk, administering 400 IU of Vitamin D daily to infants or prescribing higher doses for breastfeeding mothers might prevent deficiency. The benefits of such supplementation on bone health remain uncertain [12].

Research conducted by Tester & Capaldi[13], indicates that high-dose Vitamin D supplementation for pregnant mothers may decrease the risk of enamel defects in their children.

5. Conclusion

Vitamin D plays an important role in various metabolism and development of the human body, including the development of bones and teeth. Vitamin D deficiency can cause developmental disorders and various oral diseases such as enamel hypoplasia and can inhibit tooth development. Therefore, sufficient Vitamin D is essential, especially during pregnancy and the first years of life, to avoid deficiency diseases.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this document.

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