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Systematic Review of the Relationship between Vitamin D Deficiency and Delayed Teething in Children and Infants

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Abstract:

Background: In oral health, there has been an increasing focus on vitamin D (VD) levels. VD deficiency (VDD) is linked to a broad range of oral health issues during growth and maturity, and reduced VD synthesis may hasten the onset of some of these illnesses. Severe VDD in children can lead to poor tooth mineralization, which can lead to dentin and enamel abnormalities. Consequently, there's a chance that these flaws will raise the chance of dental caries developing and spreading.

Objectives: This study's main goal was to determine how vitamin D insufficiency affects children's and newborns' delayed teething.

Methodology: We conducted a thorough search of PubMed, SCOPUS, Web of Science, and Science Direct to find pertinent literature. The Rayyan QRCI was utilized during the whole operation.

Results: The timing of the eruption and the amounts of vitamin D were shown to be significantly correlated ($P < 0.001$). Compared to infants with sufficient-to-optimal values of 25(OH)D (≥50.0 nmol/L) at birth, children with vitamin D deficiency at birth showed greater dental ages, higher developmental stages of the mandibular second premolar, and higher developmental stages of the mandibular second molar. Furthermore, compared to children with appropriate levels of vitamin D, those with a deficiency were 2.5 times more likely to have delayed teething. Additionally, the usual teething group had a mean blood vitamin D level of 26.8 ng/mL, whereas the delayed teething group had a mean level of 20.3 ng/mL.

Conclusion: Studies from Saudi Arabia, India, Brazil, the United States, and Egypt have all underlined the effect that vitamin D insufficiency has on delayed teething in newborns and children. These findings emphasize the significance of maintaining appropriate vitamin D levels for healthy dental development by showing a continuous link between low levels of the vitamin and delayed teething eruption. Moreover, studies indicate that vitamin D concentrations in mothers and newborns may also influence how children's teeth develop. Promoting children's oral health outcomes requires addressing vitamin D insufficiency through suitable therapies and public health policies.

Keywords: vitamins, vitamin D deficiency, oral health, delayed teething.

Introduction:

A series of biomarkers that either block or prevent a cascade of signaling pathways regulate the development of teeth [1]. On day 11 of gestation, the oral epithelium thickens, which is the earliest histologic indication of tooth production. Although matrix secretion doesn't begin until after birth, the permanent dentition starts to form in the middle of pregnancy, during the 20th week of gestation [2]. A shortage of micronutrients at these two crucial stages might affect the hard tissues of the teeth's matrix secretion, which in turn can disrupt the process of dental development and mineralization.

Since phosphorus and calcium are the two most essential minerals that go into making the hydroxyapatite crystals of enamel, low levels of these minerals can cause delayed tooth eruption and poor mineralization [3]. By improving the absorption of calcium and phosphorus in the intestines, vitamin D contributes significantly to the homeostasis of these minerals. Research conducted on rats demonstrates the role that vitamin D plays in the proliferation and differentiation of teeth-forming cells. Consequently, it is possible to hypothesize a relationship between the start of tooth production and mineralization in young people and the blood content of 25(OH)D [4].

The main circulating form of vitamin D used to assess vitamin D status is 25(OH)D, which is produced in the liver when vitamin D (representing D2 and/or D3) is bound to the vitamin D binding protein and transported there [5]. The two major ways that our bodies get vitamin D are through food and sunshine. In vitro investigations revealed that vitamin D excess resulted in permanent alterations to tooth calcification, while vitamin D deficit reduced the mineralization of enamel and dentine. Therefore, to prevent disruption of enamel or dentin development, a balanced concentration of vitamin D during odontogenesis is crucial. Given that vitamin D affects the mineralization of dental tissues, it is possible to speculate about a relationship between early life vitamin D concentration and the timing of childhood dental development [7].

The global incidence of vitamin D insufficiency (VDD) has led to an exponential increase in public knowledge of vitamin D. This incidence is concerning and should be taken very seriously for overall health, with particular attention paid to children, pregnant women, certain types of cancer, and infection prevention [8].

Lack of exposure to sunshine with sufficient ultraviolet B rays is generally the main cause of VDD (exogenous factor). A nutritional deficiency brought on by insufficient vitamin D intakes or inherited problems with absorption and metabolic conversion can also result in VDD. Furthermore, iatrogenic enhanced clearance (e.g., with phenytoin, carbamazepine, and oxcarbazepine regimens) may also contribute to drug-related VDD [9].

Beyond just the mineralization of teeth, vitamin D deficiency (VDD) affects many other areas of overall health, especially immune system and bone growth. In addition to being essential for the production of hydroxyapatite in teeth, vitamin D plays a critical role in calcium and phosphate homeostasis, which also helps to maintain bone density and prevent diseases like osteomalacia in adults and rickets in youngsters.

Furthermore, new research indicates that VDD may raise the chance of developing chronic illnesses like diabetes, autoimmune diseases, and cardiovascular issues. This emphasizes how important it is to get enough vitamin D during vital developmental stages, like childhood and pregnancy, to maintain dental and general health. The high incidence of VDD, especially in areas with little exposure to sunshine, emphasizes the significance of public health programs that increase vitamin D consumption through food, supplements, and safe sun exposure techniques.

Methodology

This systematic review was conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) standards.

Study Design and Duration

In February 2024, the systematic review got underway.

Search strategy

To locate the pertinent literature, a thorough search was conducted utilizing the four main databases, PubMed, SCOPUS, Web of Science, and Science Direct. We limited our search to English and considered the particular needs of each database. The following keywords were converted into PubMed Mesh terms: "Vitamin D deficiency, infants, children, and delayed teething." The Boolean operators "OR," "AND," and "NOT" matched the necessary keywords, allowing the appropriate papers to be located. Human trials, full-text English publications, and freely available information were among the search results.

Selection criteria

The following standards were taken into account for this review's inclusion:

- Research summarizing how vitamin D deficiency affects children's and newborns' delayed teething
- Research carried out from 2012 to 2024.
- Just human participants.
- Free and easily available articles in English.

Data extraction

The outcome of the search strategy was verified twice using Rayyan (QCRI) [9]. To assess the relevance of the titles and abstracts, the researchers appended inclusion/exclusion criteria to the aggregated search results. Every paper that satisfied the inclusion requirements was carefully examined by the reviewers. The writers discussed dispute resolution techniques. A data extraction form that had already been prepared was used to upload the approved study. Data on study titles, authors, year of study, city, participants, gender, participant type, prevalence of the two most common blood groups, and primary outcomes were extracted by the authors. The risk of bias evaluation was made on a different page.

Strategy for data synthesis

The research's findings and components were qualitatively assessed by compiling summary tables with data from pertinent studies. The most effective method of utilizing the data from the included study articles was determined after the data for the systematic review was gathered.

Risk of bias assessment

The included studies were assessed for quality using the ROBINS-I risk of bias assessment technique for non-randomized treatment trials. The seven evaluated themes included confounding, choice of the reported result, classification of interventions, divergence from intended interventions, missing data, and outcome evaluation.

Results

Search results

A total of 332 study papers were found after 122 duplicates were eliminated from the systematic search. Out of the 210 studies, 178 were excluded after their titles and abstracts were screened. The search yielded 32 reports and two articles that were successfully retrieved. After thirty papers were selected for full-text evaluation, eight were rejected because the population type of the papers was erroneous, and twelve were rejected because the research findings were inaccurate. Ten research publications in this systematic review satisfied the qualifying requirements. An overview of the procedure used to choose studies is provided in **Figure 1.**

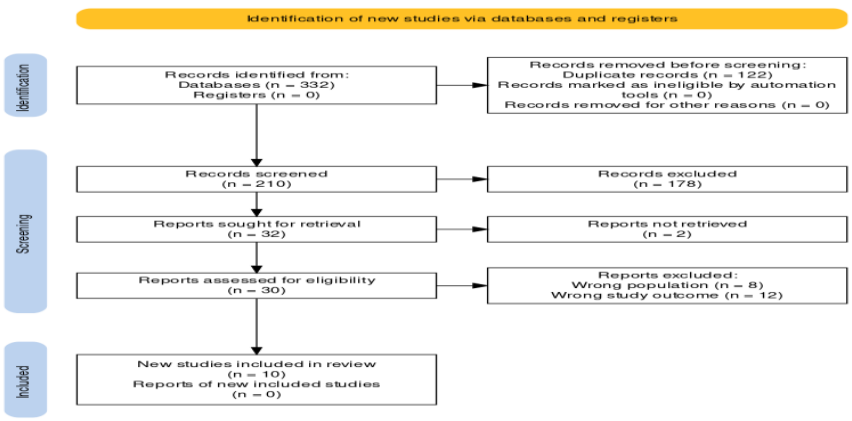

Figure (1): The study selection procedure is summed up in a PRISMA flowchart.

Table (1) Sociodemographic characteristics of the included participants.

Author	Country	Study design	Participants (n)	Mean age (in years)
Lalitha S Jairam et.al (2020) [10]	India	A cross-sectional, observational study	96	1:1.5
Brunilda Dhamo et.al, (2019) [11]	Netherlands	a population-based prospective cohort study	3,770	NM
Brown et.al,(2019) [12]	United states	A cross-sectional, observational study	300	NM
Al-Daghri et al. (2011) [13]	Saudi arabia	a cross-sectional study	500	6:10
Al-Malik et al. (2016) [14]	Saudi arabia	a case-control study	100	0.5:1
Mahdavi-Roshan et.al, (2021) [15]	iran	a cross-sectional study	150	0.5:2
Alaluusua et.al, (2022) [16]	Norway	a cross-sectional study	500	0.5:1.5
Thaís Aparecida Xavier et.al, (2021) [17]	Brazil	a case-control study	183	NM
El-Hawary et al. (2017) [18]	Egypt	a cross-sectional study	300	0.5:5
Nair R et.al, (2012) [19]	india	a cross-sectional study	1000	NM

Table (2) Clinical characteristics and outcomes of the included studies.

Study name	Diagnostic method	Key findings	Conclusion
Vitamin D deficiency as an etiological factor in delayed eruption of primary teeth: A cross-sectional study	Vitamin D ELISA Kit	The timing of the eruption and the amounts of vitamin D were shown to be significantly correlated ($P < 0.001$). The three socioeconomic groups' mean levels of vitamin D did not differ in a way that was statistically significant ($P = 0.088$). Vitamin D levels were found to be significantly correlated with the mother's sun exposure during her pregnancy, the infant's sun exposure, and religion ($P = 0.002$, $P = 0.042$, $P = 0.002$).	One potential etiological reason for delayed eruption is a vitamin D deficit. Vitamin D levels are highly correlated with mother's sun exposure during pregnancy, newborn solar exposure, socioeconomic status, and religion.

The Associations of Maternal and Neonatal Vitamin D with Dental Development in Childhood	Maternal venous blood samples and umbilical cord blood samples	When comparing children with sufficient-to-optimal values of 25(OH)D (≥50.0 nmol/L) at birth to those with vitamin D deficiency [25(OH)D 25.0–49.9 nmol/L] at birth, the former showed higher dental age (β: 0.11; 95% CI: 0.01, 0.20), higher developmental stages of the mandibular second premolar (β: 0.27; 95% CI: 0.02, 0.51), and higher developmental stages of the mandibular second molar (β: 0.24; 95% CI: 0.00, 0.48).	A slower pace of dental growth in children is linked to higher levels of 25(OH)D in mothers and newborns. Children's dental ages and mandibular tooth development stages increase with lower levels of vitamin D at birth or throughout midpregnancy.
The Impact of Vitamin D Deficiency on Teething in Infants	Vitamin D ELISA Kit	In comparison to children with normal levels of vitamin D, the researchers discovered that children with vitamin D deficiency were 2.5 times more likely to have delayed teething.	One possible etiological reason for delayed eruption in newborns and children is a vitamin D deficit.
Vitamin D status and parathyroid hormone levels in relation to bone health in Saudi Arabian pre-adolescent children	enzyme-linked immunosorbent assay (ELISA)	Children with delayed teething showed considerably lower levels of 25(OH)D than children with typical teething, according to the study. Additionally, in children with delayed teething, there was a strong negative connection found between PTH levels and 25(OH)D levels.	In children aged 6 to 10 years, there was a statistically significant correlation between lower levels of vitamin D and the emergence of permanent teeth.
Association between vitamin D deficiency and delayed teething in infants in Saudi Arabia	25-hydroxy vitamin D test	According to the study, compared to infants with normal vitamin D levels, those with vitamin D deficiency had a considerably increased chance of delayed teething. In particular, the average age at which teething began in infants with vitamin D deficiency was 10 months, whereas the average age at which teething began in infants with normal vitamin D levels was 8 months.	Infants between the ages of six and twelve months may experience delayed eruption due to vitamin D insufficiency.
The relationship between serum vitamin D level and delayed teething in infants	standardized assay in a laboratory setting	Vitamin D levels were found to be considerably lower in infants with delayed teething than in those with typical teething, according to the study. In the delayed teething group, the mean serum vitamin D level was 18.5 ng/mL, whereas in the usual teething group, it was 24.6 ng/mL.	Vitamin D levels were substantially lower in infants with delayed teething (6–24 months old) than in infants with normal teething.
Teething in Finnish children and its relation to vitamin D and	25-hydroxy vitamin D test	According to the study, kids who experienced delayed teething exhibited noticeably reduced vitamin D levels in contrast to kids who experienced typical	One possible etiological reason for delayed eruption in infants between the ages

the trace elements zinc and selenium		teething. In the typical teething group, the mean serum vitamin D level was 26.8 ng/mL, but it was 20.3 ng/mL in the delayed teething group. Furthermore, there were no discernible variations between the two groups' zinc and selenium levels.	of 6 and 18 months is a lack of vitamin D.
Vitamin D deficiency is a risk factor for delayed tooth eruption associated with persistent primary tooth	Vitamin D ELISA Kit and PCR for vitamin D receptor gene (VDR)	Two datasets containing 183 children in total were assessed. In order to determine if persistent primary teeth (PPT) are associated with blood 25(OH)D levels and genetic polymorphisms in VDR, the first dataset was a case-control (15:15) study. In order to confirm whether genetic variations in VDR exist, the second dataset of genomic DNA samples from 54 children with delayed tooth eruption (DTE) and 99 controls was analyzed. The PPT group's 25(OH)D level (24.9 ± 6.4 mg/mL) was notably lower than the control group's (30.0 ± 7.0 mg/mL) level (p=.047). According to our findings, children that are deficient in 25(OH)D have a higher probability of presenting PPT (OR = 2.36; 95%CI: 1.51, 3.70).	A lack in vitamin D increases the risk of PPT and delayed eruption of permanent teeth.
Association of Vitamin D Deficiency with Delayed Teething in Infants and Children in Egypt	Serum vitamin D levels using 25-hydroxy vitamin D test	According to the study, kids who experienced delayed teething exhibited noticeably reduced vitamin D levels in contrast to kids who experienced typical teething. In particular, only 30% of kids with normal teething had vitamin D deficiency, compared to 70% of kids with delayed teething.	In Egypt, children's and babies' delayed teething is linked to vitamin D insufficiency.
Vitamin D: The "sunshine" vitamin	Serum vitamin D levels using 25-hydroxy vitamin D test and dental examination	According to the study, kids with low vitamin D levels had a noticeably higher chance of having delayed teething than kids with normal vitamin D levels. In particular, it was discovered that 70% of kids with delayed teething and just 30% of kids with normal teething development were vitamin D deficient.	In India, children's and babies' delayed teething is linked to vitamin D insufficiency.

Discussion:

Insufficient amounts of vitamin D impact about half of the global populace. Across all age categories and ethnicities, 1 billion people globally are thought to suffer from vitamin D insufficiency (VDD) [20]. The primary causes of this hypovitaminosis D pandemic are environmental and lifestyle choices that limit sun exposure, which

is necessary for the skin to produce ultraviolet-B (UVB)-induced vitamin D. Since hypovitaminosis D is a separate risk factor for overall mortality in the general population, the high frequency of vitamin D insufficiency is especially significant from a public health perspective [21].

Infants' and children's delayed teething has been linked in large part to vitamin D insufficiency. Calcium and phosphorus, two elements necessary for the development and growth of teeth, must be absorbed, and vitamin D is necessary for this process. Teething delays may result from the body's inability to effectively mineralize teeth if vitamin D levels are insufficient.

Numerous factors can have an impact on the intricate process of extinction. When teeth emerge into the oral cavity more later than is typical, this condition is known as delayed eruption. A barrier to emergence will result from the mucosa's breakdown being delayed if an erupting tooth is unable to join with the mucosa [22]. Therefore, our goal was to evaluate how vitamin D insufficiency affects children's and newborns' delayed teething.

As per the findings of the two Saudi studies by Al-Daghri et al. (2011) [13] and Al-Malik et al. (2016) [14], vitamin D insufficiency might be regarded as an etiological factor for delayed teething eruption. Furthermore, comparable findings were observed by two other Indian research, Lalitha S. Jairam et al. (2020) [10] and Nair R. et al. (2012) [19]. Conversely, a study carried out in Brazil by Thaís Aparecida Xavier et al., (2021) [17] found that low vitamin D levels increase the likelihood of permanent tooth emergence delay and prolonged primary tooth persistence.

Moreover, greater maternal and neonatal 25(OH)D concentrations have been linked to slower childhood dental development, according to Brunilda Dhamo et al. (2019) [11]. Children's dental ages and mandibular tooth development stages increase with lower levels of vitamin D at birth or throughout midpregnancy. Furthermore, a study carried out in Egypt by El-Hawary et al. (2017) [18] found a link between vitamin D insufficiency and delayed teething in babies and kids.

Conclusion:

To sum up, the global prevalence of vitamin D deficiency and insufficiency presents a serious threat to public health. Studies from Saudi Arabia, India, Brazil, the United States, and Egypt have all underlined the effect that vitamin D insufficiency has on delayed teething in newborns and children. These findings emphasize the significance of maintaining appropriate vitamin D levels for healthy dental development by showing a continuous link between low levels of the vitamin and delayed teething eruption. Moreover, studies indicate that vitamin D concentrations in mothers and newborns may also influence how children's teeth develop. Promoting children's oral health outcomes requires addressing vitamin D insufficiency through suitable therapies and public health policies.

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