BMC Oral Health

RESEARCH

Open Access

Evaluation of serum levels in children with delayed eruption

Meryem Sahin[1*] and Ismet Rezani Toptanci[2]

Abstract

Aim This study aimed to assess levels of 25-hydroxy vitamin D ($25(OH)D_3$), calcium (Ca^{+2}), phosphorus (P), and parathyroid hormone (PTH) and to determine delayed tooth eruption by examining their correlations.

Material and method The study included 101 paediatric patients, aged 6–14 years, who visited the Dicle University Paediatric Dentistry Clinic, had no systemic diseases, and had not received medication in the past three months. Among them, 60 patients exhibited delayed eruption of their permanent central and first molar teeth, while 41 did not. Serum levels of $25(OH)D_3$, Ca^{+2}, P, and PTH were measured. Statistical analyses were performed using IBM SPSS software, with statistical significance set at $p < 0.05$.

Results Serum levels of $25(OH)D_3$ and Ca^{+2} were significantly lower in the patient group, whereas PTH levels were significantly lower in the control group ($p < 0.05$). However, serum P levels did not differ significantly between the groups ($p > 0.05$).

Conclusions Serum parameters play a significant role in tooth eruption. The significance of vitamin D has increased because of its physiological effects and involvement in metabolic pathways, highlighting the need to examine Ca^{+2}, P, and PTH levels, which contribute to its regulation. Low levels of vitamin D and Ca^{+2}, along with elevated PTH levels, have been identified as potential factors contributing to delayed tooth eruption, whereas P levels do not appear to have a significant impact. In view of the ongoing growth and development in this patient group, regular monitoring of vitamin D, Ca^{+2}, and PTH levels, along with timely interventions, is essential.

Trial registration TCTR identification number: TCTR20240729001; registered on 29 July 2024. The trial was registered retrospectively.

Keywords Eruption, Vitamin D, Parathyroid hormone, Calcium, Phosphorus

Introduction

Tooth eruption is an intricate process involving the coordination of various genetic, molecular, environmental, cellular, and tissue factors, which contribute to differences in eruption timing [14]. Teeth erupt across a wide range of chronological ages, and factors such as ethnicity, race, sex, and individual characteristics affect eruption timing, informing the standardisation of normal eruption periods [22, 24]. Although eruption times vary among individuals during both primary and permanent dentition periods, deviations within six months are considered normal. A tooth is considered to exhibit delayed tooth eruption (DTE) if its eruption time exceeds two standard deviations from the mean of established norms [27]. Early eruptions have also been documented, but DTE is the most common deviation. DTE is defined as the failure of a tooth to appear in the oral environment within the expected timeframe, owing to factors other than sex and

*Correspondence:
Meryem Sahin
meryem.sahin@mersin.edu.tr
[1] Department of Pediatric Dentistry, Faculty of Dentistry, Mersin University, Mersin, Turkey
[2] Department of Pediatric Dentistry, Faculty of Dentistry, Dicle University, Diyarbakır, Turkey

ethnicity. Chronological age is most often used to define DTE, and although it does not always reflect biological age, it provides a basis for assessing normal eruption timing in clinical evaluations [37].

In clinical practice, significant deviations from established norms in eruption timing are frequently observed. DTE may often be the primary or only symptom of underlying local or systemic pathology [29]. Nutritional status, particularly deficiencies or excesses of vitamins and minerals during developmental stages, can affect dental hard tissue [25]. Endocrine gland disorders can also have a substantial impact on the entire body, including the teeth. Hypothyroidism, hypopituitarism, hypoparathyroidism, and pseudo-hypoparathyroidism are the most common endocrine disorders associated with DTE [33].

Vitamin D can exert effects distant from its site of synthesis and is regulated through feedback control. It is hydroxylated in the liver by 25-hydroxylase (25-OHase) to produce 25-hydroxy vitamin D_3 ($25(OH)D_3$) [12]. Plasma $25(OH)D_3$ levels provide a reliable measure of vitamin D status. Although this form is not biologically active in blood circulation, it serves as a dependable parameter [31]. The biologically active form of vitamin D, 1,25-dihydroxy vitamin D_3 ($1,25(OH)_2D_3$), also known as calcitriol, is produced by the enzyme 1α-hydroxylase [4]. However, because of its short half-life, it is not considered a reliable indicator of overall vitamin D status [17].

Long-term vitamin D deficiency results in decreased serum calcium (Ca^{+2}) levels and increased release of parathyroid hormone (PTH), leading to reduced mineralisation of the collagen matrix [1]. The primary function of active vitamin D, produced by the kidneys and acting as a steroid hormone, is to regulate bone mineralisation. Vitamin D is essential for the absorption of Ca^{+2}, magnesium (Mg), and phosphorus (P) in the intestines, all of which are necessary for proper bone and tooth mineralisation [7]. PTH, regulated by blood Ca^{+2} levels, plays a role in tooth eruption by mediating signalling between osteoblasts and osteoclasts in the dental follicle and alveolar bone [3, 36]. Studies on the interaction between PTH and its receptor (PTH1R) during tooth eruption indicate that genetic alterations in PTH1R are associated with DTE [30]. PTH serves as the primary regulator of bone and mineral metabolism, balancing Ca^{+2} and P levels. The synthesis and secretion of PTH are largely regulated by Ca^{+2} levels [12]. In addition, elevated serum P levels stimulate the release of PTH [35]. PTH activates 1α-hydroxylase, which converts the inactive form of vitamin D, $25(OH)D_3$, to its active form, $1,25(OH)_2D_3$ [19]. P is the second-most abundant mineral in the body after Ca^{+2}, yet it is more widely distributed and serves various biological functions. In the blood, P exists as phosphate, but its levels are measured as elemental P [32]. When $25(OH)D_3$ levels fall below a critical threshold or Ca^{+2} absorption from the intestines is insufficient, PTH levels rise, resulting in secondary hyperparathyroidism. Under the influence of PTH, 1α-hydroxylase is activated, increasing $1,25(OH)_2D_3$ levels and promoting bone metabolism of Ca^{+2} [34].

DTE, if not diagnosed promptly, can lead to long-term complications, including orthodontic issues, malocclusion, and jaw structure disorders. Investigating the biochemical parameters that influence bone metabolism and tooth eruption is therefore critical to understanding the biological mechanisms underlying this delay. Serum parameters and their relationships provide insights into bone metabolism. To our knowledge, this is the first study to examine the relationship between DTE and serum parameters in light of the effects of bone metabolism on the eruption mechanism through apposition and resorption. This study is significant because DTE can often be the primary or only symptom of local or systemic pathology, and identifying potential orthodontic issues and their timing may help prevent complications. Because bone metabolism directly impacts orthodontic movements via apposition and resorption, DTE can influence treatment indications, plans, and timing for orthodontic patients. Consequently, DTE can have considerable implications for the health screening of patients, underscoring the importance of this study.

This study aimed to determine how insufficient levels of $25(OH)D_3$ affect Ca^{+2} and P balance and its relationship with PTH in cases of DTE. Identifying the critical point at which PTH levels deviate according to $25(OH)D_3$ levels, as well as the borderline levels of vitamin D insufficiency and deficiency, is essential in relation to eruption timing. This study specifically aimed to evaluate differences in serum $25(OH)D_3$, PTH, Ca^{+2}, and P levels, which are hypothesised to contribute to delayed eruption of permanent central and first molar teeth in children aged 6–14 years. Moreover, it sought to explore the relationships between these factors by comparing blood samples from patients within a similar age range.

Material and method

This cross-sectional study received approval from the Dicle University Faculty of Dentistry Local Ethics Committee, with the decision dated 27 January 2021 (No. 2021-09). It was supported by the Dicle University Scientific Research Project Coordination Office (Project No. DIS.21.004). This human observational study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines and was conducted in accordance with the Declaration of Helsinki. As all participants were under 16 years of age, written

informed consent was obtained from their parents or legal guardians.

A total of 101 randomly selected paediatric patients, aged 6 to 14 years, who visited the Department of Paediatric Dentistry at Dicle University Faculty of Dentistry, were included in the study. Sixty patients had delayed eruption of permanent central and first molar teeth, while 41 did not. DTE was diagnosed through clinical examination and radiographic evaluation using standardised protocols. The mean age of eruption was compared with established norms from population studies. To ensure consistency and standardisation, all evaluations were conducted by a single clinician.

Sociodemographic information and medical history were recorded in a patient information file during the examination. Children in both the patient and control groups were selected to have similar sociodemographic characteristics, with attention given to achieving comparable sex distributions. Patients having no systemic disease, had not used antibiotics in the past three months, and had not received oncological or endocrinological treatment for conditions such as asthma or chronic kidney disease (CKD) were selected. Children who did not meet these criteria were excluded from the study.

Vitamin D deficiency is commonly observed in children. To assess this deficiency, it was evaluated alongside other parameters, including PTH, Ca^{+2}, and P. Given these conditions, the blood parameters in this study were routinely and frequently examined together. Blood samples were not specifically requested from patients who did not already have these tests taken as part of routine care; these patients were excluded from the study from the outset. Following clinical and radiological evaluation, blood parameters were assessed using results from blood samples taken at the Dicle University Child Health and Diseases Hospital.

The normal reference range for PTH is 10–65 pg/mL [19]. Because abnormal levels can affect vital functions, regular monitoring of blood Ca^{+2} levels is essential. Total plasma Ca^{+2} concentration should range between 2.2 and 2.6 mmol/L (8.8–10.4 mg/dL). In blood, P exists as phosphate, although its concentration is measured as elemental P, with a normal range of 2.5–4.5 mg/dL. The regulation of P levels is less strict than that of Ca^{+2}, with considerable variations secondary to dietary and nutritional factors [32]. To determine vitamin D status, serum 25(OH)D_3 levels are classified as follows: < 20 ng/mL indicates deficiency, 20–30 ng/mL insufficiency, 30–44 ng/mL sufficient, and 50–70 ng/mL optimal. Levels above 150 ng/mL are considered toxic [11]. Serum 25(OH)D_3 levels fluctuate seasonally, generally increasing in summer and decreasing in winter [2]. This study was conducted in spring to assess vitamin D levels. Serum 25(OH)D_3, PTH, Ca^{+2}, and P levels of both the patient and control groups were analysed to identify disparities and assess correlations.

This study had a 5% margin of error, a 95% confidence level, a high effect size, 101 samples divided into two groups (n1 = 60, n2 = 41), and 99% power. The analysis was conducted using the GPower 3.1 software package.

Statistical analysis was performed using IBM SPSS version 21. Shapiro-Wilk and Kolmogorov-Smirnov tests were applied to assess the normality of variable distribution. In view of the total sample size of 101, with each group exceeding 30 samples, the Kolmogorov-Smirnov test was selected to evaluate the distribution. As the data did not follow a normal distribution, the non-parametric Mann-Whitney U test was used for group comparisons. The chi-square test was employed to examine relationships among categorical variables, as well as to assess the homogeneity of distribution between the patient and control groups by sex. The relationship among all groups was calculated using the chi-square test, based on expected and observed values. The significance level was set at $p < 0.05$.

Results

A total of 101 paediatric patients who visited the Department of Paediatric Dentistry at Dicle University Faculty of Dentistry, where they underwent clinical and radiological examinations, were included in the study. The patient group included 60 patients (36 males and 24 females) with delayed eruptions, whereas the control group comprised 41 patients (22 males and 19 females) without delayed eruptions (Table 1).

The average age of the patient group was 8.17 years, whereas the average age of the control group was 8.76 years. A significant difference in age was observed between the groups ($p < 0.05$; Table 2).

The mean 25(OH)D_3 level in the patient group was 8.24 ng/mL, significantly lower than that in the control group, which had a mean of 30.74 ng/mL ($p < 0.05$). The mean PTH level in the control group was 50.54 pg/mL, significantly lower than that in the patient group, which had a mean of 74.15 pg/mL ($p < 0.05$). The mean Ca^{+2} level in the patient group was 7.87 mg/dL, significantly lower than that in the control group, which had a mean of 9.62 mg/dL ($p < 0.05$). The mean P level was 4.80 mg/dL in the control group and 4.81 mg/dL in the patient group; although it was slightly lower in the control group, no significant difference was observed between the groups ($p > 0.05$; Table 3).

Table 1 Relationship between groups and gender

		Group						Chi-Squared test	
		Patient		Control		Total			
		n	%	n	%	n	%	Chi-square	p
Gender	**Male**	36	60	22	53.7	58	57.4	0.401	**0.527**
	Female	24	40	19	46.3	43	42.6		
	Total	60	100	41	100	101	100		

Table 2 Relationship between groups and age

		Group						Mann-Whitney U test		
		n	Mean	Median	Min	Max	SD	Mean rank	z	p
Age	**Patient**	60	8.17	8	7	10	0.78	45.33	−2.48	**0.013**
	Control	41	8.76	9	7	11	1.24	59.29		
	Total	101	8.41	8	7	11	1.03			

Table 3 Relationship between groups and serum parameters

		Group						Mann-Whitney U test		
		n	Mean	Median	Min	Max	SD	Mean rank	z	p
25(OH)D_3	**Patient**	60	8.24	8.23	5.68	13.47	1.67	30.5	−8.506	**0.001**
	Control	41	30.47	28.61	20.01	48.08	7.37	81		
	Total	101	17.27	9.66	5.68	48.08	11.99			
PTH	**Patient**	60	74.15	68.5	5.8	157	24.72	65.28	−5.929	**0.001**
	Control	41	50.54	48	32	81	11.66	30.1		
	Total	101	64.56	61	5.8	157	23.46			
Ca^{+2}	**Patient**	60	7.87	8	6	10.2	1.1	34.03	−7.049	**0.001**
	Control	41	9.62	9.7	8.2	10.7	0.54	75.84		
	Total	101	8.58	8.76	6	10.7	1.26			
P	**Patient**	60	4.81	4.9	3.67	6	0.56	51.29	−0.121	**0.904**
	Control	41	4.8	4.8	4.01	5.41	0.37	50.57		
	Total	101	4.81	4.84	3.67	6	0.49			

Discussion

Tooth movement occurs alongside bone resorption through osteoclastic activity in the pressure zone and bone formation via osteoblastic activity in the tension zone. Serum levels of vitamin D, PTH, Ca^{+2}, and P, regulated by feedback mechanisms, are balanced and interrelated. These elements play active roles in alveolar bone resorption and eruption path formation [23]. Consequently, this study examined the relationship between tooth eruption and the vitamins, minerals, and hormones that influence bone mechanisms.

When serum 25(OH)D_3 levels decrease, intestinal absorption of Ca^{+2} and P also declines. This reduction in absorption leads to inadequate mineralisation of the epiphyseal cartilage, making it difficult to maintain serum Ca^{+2} levels. As 25(OH)D_3 levels fall below a certain threshold, PTH secretion increases in response to low Ca^{+2} levels. The body then mobilises Ca^{+2} from the bones under the influence of PTH and 1,25$(OH)_2D_3$ to restore serum Ca^{+2} balance. Rising PTH levels further accelerate the decline in P levels. As Ca^{+2} is drawn from the bones, mineralisation of the epiphyseal cartilage decreases, and mineral content in other bone areas diminishes. Over time, clinical and biochemical signs emerge, and eventually, the serum Ca^{+2} balance cannot be maintained, even with the effects of PTH and 1,25$(OH)_2D_3$ [1].

In this study, an age difference was observed between the patient and control groups, with the control group

having a higher average age. This difference stems from the chronological age data and the random selection of patients. Similar studies have investigated $25(OH)D_3$ levels in children. For example, Haq et al. [9] analysed $25(OH)D_3$ levels in children aged 4–15 years. Xavier et al. [37] also examined vitamin D levels in 183 children aged 6–13 years with persistent primary teeth and delayed eruptions. Moreover, Kim et al. [18] investigated the relationship between tooth decay and vitamin D levels in 1,688 children aged 10–12 years.

Numerous animal model studies have shown that the local application of vitamin D accelerates tooth movement, whereas vitamin D deficiency appears to slow it down, potentially leading to delayed treatment or complications [23]. In a study on delayed eruption, Xavier et al. [37] found that the serum $25(OH)D_3$ level in a group with persistent primary teeth was significantly lower than that in the control group, suggesting that vitamin D deficiency may contribute to delayed eruptions in children. In addition, Dhamo et al. [6] reported that low vitamin D levels during birth and the second trimester of pregnancy were associated with delayed eruption of primary teeth. Crincoli et al. [5] investigated the relationship between impacted mandibular third molars and vitamin D deficiency, finding that $25(OH)D_3$ levels were low in the patient group. Their hypothesis was further supported in patients with bilateral impaction, where a clear delay in eruption was observed in those with significantly lower serum $25(OH)D_3$ levels, potentially leading to several negative outcomes. Reduced vitamin D levels may result in clinical eruption delays, orthodontic complications, and challenges in dental age determination [37].

PTH is the primary regulator of bone and mineral metabolism, maintaining the balance of Ca^{+2} and P. The amino-terminal domain of PTH binds to PTH1R on osteoblasts and osteocytes in bone, periodontal ligament cells, cementoblasts, and renal tubular cells. PTH is crucial for homeostasis in mineralised tissues. Its most important role in tooth development is regulating bone resorption and apposition during eruption. This effect is particularly significant in the mandible, which is more mineralised than the maxilla. Studies have shown that genetic changes in PTH1R are associated with failed tooth eruption by examining the interaction of PTH with its receptor during eruption [35]. During tooth development, dental follicle cells differentiate into osteoblasts, interacting with the Hertwig epithelial root sheath to form alveolar bone around tooth roots. They also recruit and activate osteoclasts to facilitate tooth development and eruption. Concurrently, parathyroid hormone-related peptide (PTHrP) is expressed around the developing tooth germ [38]. Philbrick et al. [26] reported that PTHrP plays a critical role in tooth eruption, showing that the absence of PTHrP in mice disrupts eruption—one of the first definitive studies demonstrating the role of PTH in this process. In addition, patients with elevated PTH levels showed a significant delay in tooth eruption.

If dietary Ca^{+2} is considered a threshold nutrient, as suggested by Heaney, higher serum $25(OH)D_3$ levels improve Ca^{+2} absorption [10]. With sufficient vitamin D supplementation, the threshold for optimal Ca^{+2} absorption can be met with lower Ca^{+2} intake. In a study by Hanna et al. [8], the effect of mutations in vitamin D receptors (VDR) on tooth development and timing was investigated. Observed outcomes included persistent hypocalcaemia, elevated $1,25(OH)_2D_3$ levels, developmental delays, weakened dentin structure, hypomineralisation, and early tooth loss. Similarly, Malloy et al. [21] reported that any VDR mutation results in decreased serum Ca^{+2} levels, increased PTH secretion, elevated osteoclastic activity, and higher alkaline phosphatase levels. In cases of vitamin D deficiency, hypoparathyroidism is associated with DTE, as PTH secretion increases until $25(OH)D_3$ levels are sufficient. In contrast, hyperparathyroidism is linked to elevated alkaline phosphatase, which plays a critical role in tooth maturation by enhancing calcification rates [15]. In this study, Ca^{+2} levels were significantly reduced in the patient group, alongside decreased vitamin D levels and delayed eruption. However, because the patients did not have advanced vitamin D deficiency, these conditions were not specifically analysed. Owing to the direct effects of vitamin D on Ca^{+2} metabolism, low blood Ca^{+2} levels were observed.

In a five-year follow-up of a case of hypoparathyroidism by Kelly et al. [16], increased serum P levels were observed, along with DTE and hypoplastic enamel. Similar studies have suggested that hyperphosphataemia may be a secondary factor in various eruption disturbances [13, 28]. In the present study, no significant differences in serum P levels were found between the groups. As the patients had no systemic diseases, the lack of difference in serum P levels between the groups was likely attributable to dietary and nutritional factors.

While vitamin D is activated by 1α-hydroxylase in the kidney, Ca^{+2} is also absorbed from the intestines. In a study conducted by Liu et al. [20], researchers found that mineral density in the teeth and alveolar bone of mice with 1α-hydroxylase deficiency was reduced. They also observed hypocalcaemia, hypophosphataemia, and hyperparathyroidism. The study concluded that $1,25(OH)_2D_3$ plays an anabolic role in both dentin and alveolar bone, similar to its role in long bones, whereas PTH is more effective in long bones than in the mandibular bone [20].

In a study by Sun et al. [34], the calcium-sensing receptor (CaR) was found to play a crucial role in tooth

formation and alveolar bone development in the mandible. Mice with CaR disruption exhibited hypercalcaemia, hypophosphataemia, and elevated serum PTH levels. Furthermore, the volume of teeth and alveolar bone decreased significantly, and the ratio of predentin area to total dentin increased markedly.

Consistent with other recent studies, serum parameters were found to play a significant role in tooth eruption. The importance of vitamin D has increased because of its physiological effects and involvement in various metabolic pathways. In addition, serum levels of Ca^{+2}, P, and PTH, which are involved in vitamin D regulation, should be examined. One limitation of this study was the statistically significant age difference between the groups. Therefore, conducting studies with larger and more age-matched groups is essential for a better understanding of these relationships and to draw more definitive conclusions.

Conclusions

This study aimed to determine the effects of vitamins and minerals on bone metabolism and the underlying mechanisms. Serum levels of $25(OH)D_3$, PTH, Ca^{+2}, and P, regulated by feedback mechanisms, play active roles in alveolar bone resorption and eruption path formation by maintaining a balanced state. Therefore, any eruption disorder secondary to disruptions in this cycle, potentially caused by systemic disease, can be clinically diagnosed, evaluated, and managed effectively. Recognising the significant impact of vitamin and mineral deficiencies or excesses on oral, dental, and overall health is clinically important. In this study, low levels of $25(OH)D_3$ and Ca^{+2}, with a corresponding increase in PTH levels, may have contributed to DTE; however, P levels did not appear to play a decisive role in this process. Such studies are expected to be useful reference standards for paediatric dentists, orthodontists, and paediatricians when evaluating eruption disorders in relation to bone metabolism. In cases of DTE, based on the eruption-age chart, paediatric dentists would benefit from considering serum vitamin and mineral levels in light of their effects on the eruption path.

Abbreviations

DTE	Delayed tooth eruption
25-OHase	25-hydroxylase
$25(OH)D_3$	25-hydroxy Vitamin D_3
$1,25(OH)_2D_3$	1,25-dihydroxy Vitamin D_3
PTH	Parathyroid hormone
Mg	Magnesium
P	Phosphorus
PTH1R	Parathyroid hormone receptor 1
CKD	Chronic kidney disease
PTHr-P	Parathyroid hormone-related peptide
VDR	Vitamin D receptor
CaR	Calcium-sensing receptor

Acknowledgements
Study participants are gratefully acknowledged.

Authors' contributions
MS, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript. The author gave final approval and agree to be accountable for all aspects of the work. IRT, contributed to conception, interpretation, drafted and critically revised the manuscript. The author gave final approval and agree to be accountable for all aspects of the work. All authors gave their final approval and agree to be accountable for all aspects of the work.

Funding
This study was supported by the Dicle University Scientific Research Project Coordination Office (Project number: DIS.21.004 Start date: 21.05.2021 Duration: 24 months) A Scientific Research Committee Aproval Certificate has been received from Dicle University Scientific Research Project Coordination Office.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study received ethics committee approval from Dicle University Faculty of Dentistry Local Ethics Committee with the decision dated 27.01.2021 and numbered 2021-09. Informed consent to participate was obtained from the parents or legal guardians of any participant.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 13 September 2024 Accepted: 14 November 2024
Published online: 21 November 2024

References

1. Ali N, Rahim A, Ali S, Iqbal MH. Impact of vitamin D on development of early childhood caries. Pak Armed Forces Med J. 2017;67(3):429–33.
2. Aydın A, Ilıkkan B, Haktan M, Kavunoğlu G. Doğum Sırasında Annelerdeki D Vitamini Düzeyi ve Bu Düzeylerin Mevsimlerle Iişkisi. Türk Pediatri Kongresi Kitabı. 1988;p 98.
3. Bartzela T, Türp JC, Motschall E, Maltha JC. Medication effects on the Rate of Orthodontic Tooth Movement: a systematic literature review. Am J Orthod Dentofac Orthop. 2009;135(1):16–26.
4. Combs GF Jr, McClung JP. The vitamins: Fundamental aspects in Nutrition and Health. 5th ed. Acad Press. 2016;628 p.
5. Crincoli V, Cazzolla AP, Di Comite M, Lo Muzio L, Ciavarella D, Dioguardi M, Bizzoca ME, Palmieri G, Fontana A, Giustino A, et al. Evaluation of vitamin D (25OHD), bone alkaline phosphatase (balp), serum calcium, serum phosphorus, Ionized Calcium in patients with Mandibular Third Molar Impaction. An observational study. Nutrients. 2021;13(6):1–15.
6. Dhamo B, Miliku K, Voortman T, Tiemeier H, Jaddoe V, Wolvius E, Ongkosuwito EM. The associations of maternal and neonatal vitamin D with Dental Development in Childhood. Curr Dev Nutr. 2019;3(4):1–10.
7. Dixon D, Hildebolt CF, Miley DD, Garcia MN, Pilgram TK, Couture R, Spearie CA, Civitlli R. Calcium and vitamin D use among adults in Periodontal Disease maintenance Programmes. Br Dent J. 2009;206(12):627–31.
8. Hanna AE, Sanjad S, Andary R, Nemer G, Ghafari JG. Tooth Development Associated with mutations in Hereditary vitamin D-Resistant rickets. JDR Clin Transl Res. 2018;3(1):28–34.
9. Haq A, Svobodová J, Sofi NY, Jindrová A, Kabá B, Rajah J, Anouti FA, Abdel-Wareth L, Wimalawansa SJ, Razzaque MS. Vitamin D status among the Juvenile Population: a retrospective study. J Steroid Biochem Mol Biol. 2018;175:49–54.

10. Heaney RP. The Vitamin D Requirement in Health and Disease. J Steroid Biochem Mol Biol. 2005;97(1–2):13–9.
11. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, Murad MH, Weaver CM. Evaluation, treatment, and Prevention of vitamin D Deficiency: an endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2011;96(7):1911–30.
12. Jacquillet G, Unwin RJ. Physiological regulation of phosphate by vitamin D, parathyroid hormone (PTH) and phosphate (pi). Pflügers Arch Eur J Physiol. 2019;471(1):83–98.
13. Jensen SB, Illum F, Dupont E. Nature and frequency of Dental Changes in Idiopathic Hypoparathyroidism and Pseudohypoparathyroidism. Eur J Oral Sci. 1981;89(1):26–37.
14. Juyol MH, Mechanismos Y, Teorias De La Erupción Dentaria. Estado Actual Rev Eur Odontoestomatol. 2002;14(6):349–56.
15. Kamarthi N, Venkatraman S, Patil PB. Dental findings in the diagnosis of idiopathic hypoparathyroidism. Ann Saudi Med. 2013;33(4):411–13.
16. Kelly A, Pomarico L, de Souza IPR. Cessation of Dental Development in a child with idiopathic hypoparathyroidism: a 5-Year Follow-up. Oral surgery. Oral Med Oral Pathol Oral Radiol Endodontology. 2009;107(5):673–7.
17. Khundmiri SJ, Murray RD, Lederer E, PTH, Vitamin D. Compr Physiol. 2016;6(2):561–601.
18. Kim IJ, Lee HS, Ju HJ, Na JY, Oh HW. A cross-sectional study on the Association between Vitamin D Levels and caries in the Permanent Dentition of Korean Children. BMC Oral Health. 2018;18(1):1–6.
19. Kumar R, Thompson JR. The regulation of parathyroid hormone secretion and synthesis. Am Soc Nephrol. 2011;22(2):216–24.
20. Liu H, Guo J, Wang L, Chen N, Karaplis A, Goltzman D, Miao D. Distinctive anabolic roles of 1.25-Dihydroxyvitamin D3 and parathyroid hormone in Teeth and Mandible Versus Long bones. J Endocrinol. 2009;203(2):203–13.
21. Malloy PJ, Pike JW, Feldman D. The vitamin D receptor and the syndrome of Hereditary 1,25-Dihydroxyvitamin D-Resistant rickets. Endocr Rev. 1999;20(2):156–88.
22. Massler M. The development of the human dentition. J Am Dent Assoc. 1941;28:1153–60.
23. Meikle MC. The tissue, Cellular, and Molecular Regulation of Orthodontic Tooth Movement: 100 years after Carl Sandstedt. Eur J Orthod. 2006;28(3):221–40.
24. Moorrees CFA, Fanning EA, Hunt EE Jr. Age variation of formation stages for ten permanent teeth. J Dent Res. 1963;42(6):1490–502.
25. Moynihan PJ. The Relationship between Nutrition and systematic and oral well-being in older people. J Am Dent Assoc. 2007;138(4):493–7.
26. Philbrick WM, Dreyer BE, Nakchbandi IA, Karaplis AC. Parathyroid hormone-related protein is required for tooth eruption. Proc Natl Acad Sci USA. 1998;95(20):11846–51.
27. Pinkham J, Casamassimo P, Fields HW, McTigue DJ, Nowak A. Pediatric Dentistry Infancy through Adolescence. 4th ed. Mosby. 2005;768 p.
28. Pisanty S. Primary idiopathic juvenile hypoparathyroidism. Oral surgery, oral Med. Oral Pathol. 1966;21(3):294–8.
29. Pulse CL, Moses MS, Greenman D, Rosenberg SN, Zegarelli DJ. Cherubism: Case Reports and Literature Review. Dent Today. 2001;20(11):100–3.
30. Risom L, Christoffersen L, Daugaard-Jensen J, Hove HD, Andersen HS, Andresen BS, Kreiborg S, Duno M. Identification of six Novel PTH1R mutations in families with a history of primary failure of tooth eruption. PLoS ONE. 2013;8(9):e74601.
31. Rodwell VW, Bender DA, Botham KM, Kennelly PJ. Harper's Illustrated Biochem. 2018;777 p.
32. Shaker JL, Deftos L. Calcium and Phosphate Homeostasis. Endotext. 2018.
33. Shaw L, Foster TD. Size and development of the Dentition in Endocrine Deficiency. J Pedod. 1989;13(2):155–60.
34. Sun W, Sun W, Liu J, Zhou X, Xiao Y, Karaplis A, Pollak MR, Brown E, Goldzman D, Miao D. Alterations in Phosphorus, Calcium and PTHrP contribute to defects in Dental and Dental Alveolar bone formation in calcium-sensing receptor-deficient mice. Development. 2010;137(6):985–92.
35. Vasconcelos DFP, Vasconcelos ACCG. PTH Intermittent Administration may be a useful therapeutic Agent to avoid premature eruption of the tooth. Med Hypotheses. 2016;88:27–9.
36. Wise GE, King GJ. Mechanisms of tooth eruption and Orthodontic Tooth Movement. J Dent Res. 2008;87(5):414–34.
37. Xavier TA, Madalena IR, da Silva RAB, da Silva LAB, Silva MJB, De Roosi A, Küchler EC, Fukada SY. Vitamin D Deficiency is a risk factor for delayed tooth eruption Associated with Persistent primary tooth. Acta Odontol Scand. 2021;79(8):600–5.
38. Zhang J, Liao L, Li Y, Xu Y, Guo W, Tian W, Zou S. Parathyroid hormone-related peptide(1–34) promotes tooth eruption and inhibits Osteogenesis of Dental follicle cells during tooth development. J Cell Physiol. 2019;234(7):11900–11.

Publisher's Note