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The Physiological Role of Parathyroid Hormone and Serum Calcium in Odontogenesis Stunting Children; Cross-sectional Analysis of Children Attending Dental OPD and Paediatric Ward at LUMHS

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ABSTRACT

Objectives: To determine serum PTH and serum calcium levels among children with delayed eruption of permanent teeth, attending the dental OPD at LUMHS.

Methodology: A cross-sectional study was conducted with the assistance of the Physiology Department, LUMHS, in collaboration with the Clinical Ward, Pediatric and Dental Wards, and D-R Lab, LUMHS, from March to August 2022. Children up to 18 years old, corresponding to the period of active odontogenesis and growth, diagnosed with odontogenesis stunting characterized by delayed or disrupted tooth development, as confirmed by clinical examination and radiographic imaging were included. Blood samples for PTH and serum calcium levels were obtained with the informed consent of parents. Parathyroid Hormone was considered normal from 10 to 55 picograms/ml.

Results: A total of 250 children were studied, with an overall mean age of 12.24 ± 12.0 years. Males comprised 60.4%, and females were 39.6%. Most cases (28.4%) had dentine score 0, 24.8% had dentine score I, 24.8% had dentine score II, 18.8% had dentine score IV, while only 3.2% had dentine score II. Mean parathyroid hormone levels were significantly associated with higher dentine scores ($p < 0.05$). Although mean parathyroid hormone levels were statistically insignificant according to children's age ($p < 0.05$).

Conclusion: A decrease in levels of parathyroid hormones and calcium has been observed to contribute to the delay in the eruption of primary teeth. Additionally, factors such as stunted growth and deficiencies in parathyroid hormones and calcium levels further exacerbate this delay, highlighting the importance of adequate nutrition in dental development.

Keywords: Parathyroid hormone level, calcium level, PTHrP, total protein

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Introduction

Tooth eruption involves a sequence of natural occurrences within the jawbone. It entails the emergence of the tooth's incisal edges, which push through the gum tissue and make contact with adjacent teeth in the mouth. Typically, the initial teeth begin to emerge at approximately 6 months of age, though this can vary between 4 and 9 months.[1] One reason for stunting is insufficient or diminished nutrition over an extended period, leading to interrupted growth and delayed development. Malnutrition in children under 5 is a prevalent factor contributing to disability and mortality in developing nations, potentially leading to various dietary-related disorders and an increased incidence of

cavities.[2,3] According to statistics provided by the World Health Organization (WHO), Indonesia ranks third in Southeast Asia for the prevalence of stunting. The average prevalence of stunted children under the age of five from 2005 to 2017 was 36.4%.[4] It has been reported that growth factors are pivotal for cell survival, growth, and specialization, crucial for the effective regeneration of pulp-dentin structures.[5,6] Stem cells found in dental pulp possess the ability to replicate themselves and transform into various cell types. Specifically, dental pulp cells can develop into odontoblasts, which are essential precursor cells responsible for the formation of dentin.[5,7] However, increasing evidence suggests that dental decay has adverse effects on the nutritional status and development of children. However, the precise nature of this connection remains contentious, regarding both its direction and the mechanisms involved. Recent systematic reviews indicate that certain studies have found a link between dental caries and being underweight.[8] As per the findings of the Pakistan National Nutrition Survey 2018, 40.2% of children under the age of five were affected by stunting.[9]

Stunted children often experience delayed eruption of both permanent and deciduous teeth. Malnutrition, including stunting and wasting, is frequently associated with such delays in dental development among children. Stunted children experience disruptions in this process through multiple pathways.[1,10] Factors such as calcium intake, environmental enteric dysfunction (EED), and hormonal imbalances in stunted children lead to a decrease in extracellular calcium levels in the bloodstream, constituting the first pathway. The second mechanism involves a deficiency in vitamin D and hormones, which interferes with dental pulp cell (DPC) and osteoblast cell receptor function on the cell membrane. Stunting also results in a deficiency of insulin-like growth factor 1 (IGF-1), which hampers the activity of both osteoblasts and osteoclasts in the tooth eruption process.[1,11] However, the precise reasons behind primary failure of eruption remain unidentified, although various related risk factors are present.

The rationale behind this research investigation was to gain a better understanding of the timing of permanent tooth emergence, particularly in regions like ours where a significant portion of children suffer from poverty, leading to underweight or malnutrition. This study underscores the importance of examining clinical presentations alongside dental manifestations, which enabled us to pinpoint the root cause of delayed permanent tooth eruption in children relative to their age, linked to decreased serum calcium and parathyroid hormone (PTH) levels. There are very limited studies in Pakistan documenting delayed permanent tooth development attributed to factors such as low body mass, malnutrition, recurrent infections, and inadequate social stimulation in relation to serum calcium and PTH levels. Consequently, this research offers valuable insights and presents an opportunity for local researchers to explore eruption patterns among children of various ethnic and racial backgrounds, given the diverse ethnic composition of our country.

Methodology

This descriptive cross-sectional study was conducted at the Department of Physiology in collaboration with the Department of Dentistry at LUMHS, Jamshoro. The study spanned six months after obtaining approval from the ERC LUMHS. A sample size of 250 patients was determined using the Epi Info software method, with a 5% margin of error and a 95% confidence interval. The incidence of hypocalcemia among children in Pakistan was considered to be 68.3%. All participants meeting the inclusion criteria were selected, which included children aged between 6 and 12 years, in mixed dentition, and those visiting the dental outpatient department (OPD) at LUMHS. Participants with supernumerary teeth or a history of congenital and systemic disorders were excluded. Clinical examinations were conducted under adequate lighting conditions using a wooden spatula to retract soft tissue, and the status of permanent tooth eruption was recorded. Any part of the tooth emerging or erupting in the oral cavity was considered as a tooth eruption. Blood samples for serum calcium and parathyroid hormone (PTH) were obtained following standard protocols under the supervision of well-trained nursing staff, with the ethical approval of parents being the top priority. PTH levels within the range of 10-65 pg/mL in the blood serum of children with delayed eruption were considered normal, and calcium levels within the range of 8.5-10.5 mg/dL in the blood serum of children with delayed eruption were considered normal. The study aims and objectives were explained to the participants or their guardians. The research data were recorded using a pre-designed form, and data analysis was performed using SPSS version 26.

Results

A total of 250 children were studied to determine the association of serum calcium in delayed eruption of permanent teeth among children. Mean age of the children was 12.24+ 12.0 years. Out of all study subjects' males

were in majority 60.4% and female sewer 39.6%. In this study most of the children 45.2% had history of weaning time was 1 year, 29.6% had history of weaning time was 2 years, while 25.2% had history of weaning time was 6 months. As per dentine score, most of the cases 28.4% had dentine score 0, 24.8% had dentine score 1, 24.8% had dentine score 2, 18.8% had dentine score 3, while only 3.2% ha dentine score 4. (Table I)

Table I: Descriptive statistics of baseline characteristics and dentine score. (n=250)

Variables		Statistics	
Age	Mean± SD	12.24± 3.54	
MAUC	Mean± SD	14.91±3.90	
Gender	Males	151	60.4%
	Females	99	39.6%
Weaning time	6 Months	63	25.2
	1 Year	113	45.2
	2 Years	74	29.6
Dentine score	0	71	28.4%
	1	62	24.8%
	2	62	24.8%
	3	47	18.8%
	4	8	3.2%

In this study overall mean calcium level was 7.98+1.10mg/dl and mean parathyroid hormone was 18.90+22.78 pg/ml. Furthermore, Statistical analysis indicates significant differences in both serum calcium and parathyroid hormone levels across dentine scores (p-values of 0.001 and 0.024, respectively), suggesting an association between dentine score and these biochemical markers as shown in table II.

Table II: Mean calcium and parathyroid hormones according to dentine score. (n=250)

Variables	Dentine score	N	Mean	SD	p-value
Serum calcium	0	71	7.76	1.15	0.001
	1	62	7.63	0.85	
	2	62	8.24	1.08	
	3	47	8.16	1.12	
	4	8	9.50	0.00	
	Overall	250	6.98	1.10	
Parathyroid Hormone	0	71	21.73	22.43	0.024
	1	62	7.91	2.04	
	2	62	6.11	1.83	
	3	47	11.17	17.02	
	4	8	9.70	12.18	
	Overall	250	12.90	22.78	

Discussion

Tooth eruption is a intricate process where the tooth germ emerges within the oral cavity in a synchronized manner, utilizing the available space effectively.[12] These processes are characterized by the emergence of the incisal edges of the teeth, which emerge through the gums into the oral cavity and make contact with the adjacent teeth. The initial teeth typically emerge between 4 and 9 months of age, with an average timing of around 6 months. This study has been done to determine the association of serum calcium in delayed eruption of Permanent Teeth among children and a total of 250 children were studied to determine the association of serum calcium in delayed eruption of permanent teeth among children. In this study the mean age of the children in our study was 12.24±12.0 years, with males comprising the majority at 60.4%. This finding is consistent with the study conducted by Hassan et al[12], where the age range was from 5 to 15 years, with 10 years being the most common age (19%). In the study by Hassan et al,13 reported that the mean age was reported as 9.86±2.057 years, with an equal distribution of male and female subjects (150 each).

Similarly, Bawazir et al[14] reported that among the individuals reviewed, there were 47.1% males and 52.9% females, with 20 cases identified with delayed eruption of the upper permanent first molars. Our study aligns closely with these findings. Additionally, Bayrak et al[15] also reported similar results to our study, where out of 1,491 children assessed over a six-month period, 773 were girls with an average age of 9.06±2.04 years, and 718 were boys with an average age of 8.98±2.05 years.

In this study, the mean calcium level was 7.98 ± 1.10 mg/dL and the mean parathyroid hormone level was 18.90 ± 22.78 pg/mL. Both mean calcium and parathyroid hormone levels showed significant associations with higher dentine scores ($p < 0.05$), while lower mean calcium and parathyroid hormone levels were significantly associated with bone deformities ($p < 0.05$). Moreover, calcium was identified as a key factor, as a negative significant correlation was observed between calcium levels and parathyroid hormone levels. In line with our findings, Nelwan et al,[1] noted that children with stunted growth experienced reduced levels of PTHrP, which impacted the eruption of deciduous teeth.

Similarly, decreased levels of PTHrP and vitamin D led to delayed primary tooth eruption by reducing blood calcium levels and affecting osteoblasts and osteoclasts.[1] Furthermore, a case report by Kelly et al,[16] described a 9-year-old child who remained undiagnosed with hypoparathyroidism for 6 years. The child exhibited enamel hypoplasia, incomplete root formation, and delayed tooth eruption in the permanent dentition, all attributed to untreated hypocalcemia during tooth development.[16] In comparison to our findings, study by Tedjosasongko et al,[17] revealed significantly lower levels

of PTHrP, sIgA, and total protein in the saliva of the treatment group compared to the control group ($p < 0.05$). However, in contrast to our results, Wulandari et al,[18] found no significant correlation between calcium intake and delayed eruption of permanent canines, with a p-value exceeding 0.05. Although our findings are supported by a literature review-based study by Wardani S et al,[19] which reported that out of 3,500 children examined, 13.4% were identified as stunted, and 25% were found to have thyroid disorders. This literature review-based study suggested a link between thyroid disorders and the prevalence of stunting among children.[19] Though, our study has several limitations, including a limited sample size. Therefore, we recommend further large-scale studies to validate our findings and provide more comprehensive insights into the relationship between dental health, calcium intake, and systemic health factors such as thyroid disorders.

Conclusion

In conclusion, the decrease in parathyroid hormone and calcium levels has been associated with delayed primary tooth eruption, potentially influenced by stunted growth and deficiencies in these essential nutrients. This emphasizes the crucial role of adequate nutrition in dental development. Further research is recommended to investigate the mechanisms underlying these associations and to explore interventions aimed at addressing nutritional deficiencies to enhance optimal dental health in children.

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