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Frequency of Hypovitaminosis D in Children with Growing Pains

Shah Nawaz [a] Sara Yar Khan [b] Neelam Ayub [c]
Kalsoom Tariq [d] Sikandar Ali Khan [e] Bashir Khan [f]

Abstract: *Objective: To determine the frequency of Hypovitaminosis D in kids by increasing pains and to find out the relationships among biochemical biomarkers and serum vitamin D concentration levels. Study Design: An exploratory cross-sectional investigation was conducted. Methodology: Growing pains were diagnosed in 100 outpatient children aged 5–12 with diffuse lower leg pains. The study excluded infants with arthritis, systemic diseases, organic pain, rheumatologic diseases, or rickets symptoms. We measured total inorganic phosphate, calcium, alkaline phosphatase, and vitamin D3 (25-hydroxycholecalciferol). Group A had enough vitamin D3 (> 75 nmol/L), Group B had 50–75, and Group C had levels below 50. Group rates mattered at 0.05 in the chi-square test. Results: 9-year-olds and 60% women participated. 7% of infants with growth pains had enough vitamin D. 95% of vitamin D-deficient babies had high alkaline phosphatase. Conclusion: Growth pains may cause hypovitaminosis D. Youngster's Vitamin D levels should be tested for unusual leg pain. Molecular clues cannot diagnose hypovitaminosis D.*

Key Words: Vitamin D, Growing Pains, Vitamin D3, Hypovitaminosis D

Introduction

One of the most common clinical terms is "growing pains" (GP), which are thought to occur in 25% to 40% of children who have no underlying disease (Ahmed 2022). The common clinical features of GP include being non-articular, typically bilateral, and occurring in the shins, calves, thighs, or popliteal fossa. Pain typically strikes in the evening or at night, and its severity can range from very minor to really severe. The time spans between minutes and hours. When they are hugged, rubbed, and snuggled, children, feel better. Almost invariably, it becomes better by morning. Physical examination reveals zero obvious indications of inflammation. Children between the ages (of 9 and 12) who are otherwise healthy tend to have GP, while they can also occur in younger ages as well (Ali 2022).

French doctor Marcel Duchamp coined the term GP in the medical nomenclature for the first time in 1823. It is still a poorly known disease entity nearly 200 years later. There haven't been many investigations to clarify the biology and etiology of this widespread condition. GP may be

[a] Associate Professor, Department of Biochemistry, Nowshera Medical College, Nowshera, KP, Pakistan.
[b] Senior Lecturer, Department of Biochemistry, Jinnah Medical College, Peshawar, KP, Pakistan.
[c] Senior Registrar, Department of Dermatology, Rawal Institute of Health Sciences, Islamabad, Pakistan.
[d] Assistant Professor, Department of Biochemistry, Khyber Girls Medical College, Peshawar, KP, Pakistan.
Email: drkalsoomtariqyahoo.com *(Corresponding Author)*
[e] Lecturer, Department of Biochemistry, Khyber Girls Medical College, Peshawar, KP, Pakistan.
[f] Assistant Professor, Department of Biochemistry, Pak International Medical College, Hayatabad, Peshawar, KP, Pakistan.

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brought on by stress on muscles connected to growing bones, according to certain theories. These muscles could be weak and painful (Bughio 2020).

GP in children might result in a poor pain threshold and weakened bones. The youngster may be more susceptible to developing pains due to a number of psychological and familial variables. Recently, the theory of mechanical stress brought on by poor foot posture, flat feet, and developing pains has been undermined (Čulić 2021). Joint hyper mobility and other parameters, such as blood perfusion abnormalities, were examined, but no definitive findings were made (Dijkstra 2023).

One study indicated that the calcium consumption of GP patients in the group with reduced bone strength was considerably low. Although this notion has not been tested, a diet rich in vitamin D (Vit D), as well as calcium, was thought to affect both bone development and pain experiences. Maintaining healthy calcium absorption is Vit D primary goal. The entire phosphorus and calcium absorbed by the intestine are increased by Vit D from 10–20% and 60% to 30–40% and 80%, respectively (Fernandes 2023, Habib 2020).

Serum calcium levels are the first to decrease in the presence of hypovitaminosis D, while phosphorus levels are kept within the normal range. The secondary hyperparathyroidism that results from this hypocalcemia raises the blood level of vitamin D3, decreases the quantity of plasma phosphorus, and restores normal levels of calcium in the body (Huang 2020, Jeyakumar 2019).

With PTH-induced bone resorption, which also raises the alkaline phosphatase level in the blood, this balance is reached. If untreated, this disease eventually causes bone stores to run out and hypocalcemia to reoccur. Studies demonstrating the part a Vit D deficiency plays in the pathophysiology of developing pains are not readily available (Kanta 2019, Karim 2020).

This study sought to examine the association between blood Vit D levels and common biochemical markers in growing children and estimate the levels of Vit D in their serum.

Methodology

This study was conducted at the Nowshera Medical College, from September 2021 to June 2022. For the study, 100 children between the ages of 5 and 12 who had limb discomfort and were enlisted matched the diagnostic standards for growing discomfort. Kids with rheumatologic issues, organic discomfort, or any form of systemic ailment, overt rickets symptoms, and malnutrition were disqualified. Parental permission was secured in writing. The questions about milk consumption and demographic graphics factors were asked on a pre-designed questionnaire. ALP, vitamin D3/25-hydroxycholecalciferol (25-OHD), calcium (Ca), phosphorus (PO), and alkaline phosphatase (ALP) serum concentrations were tested.

Each assay was conducted in accordance with the manufacturer's guidelines. The laboratory standard ranges for Ca and PO were 2.3-2.75 and 0.8-1.9 mmol/L (respectively) in women and 0.97-1.94 mmol/L in men (7-12 years), and ALP 269 U/L (4-6 years) and 300 U/L. Three distinct levels of vit D were determined: acceptable, inadequate and poor (>75 nmol/L, 50-75 nmol/L, and 50 nmol/L) respectively.

Based on the participants' serum 25-OHD concentrations, three categories were created: group 1 had reasonable levels, group 2 had inadequacy, and group 3 had quite a vitamin D3 deficit.

SPSS version 13 was used to analyse the data. Numerical data were presented as averages and standard deviations, whilst qualitative characteristics were portrayed as percentages. The correlation between calcium, serum 25-OHD and ALP was evaluated utilizing a chi-square test. A p-value of 0.05 or less was used to determine statistical significance.

Results

100 patient with age between 5 to 12 years were examined. The participants average age was 9.05 + 3.19 years. In the research group, there were 42% boys and 60% girls. 17% of participants drank milk that had been fortified with vit D, and the average child drank 0.45 L (0.22 L) of milk daily. Table I gives mean values for serum calcium, phosphorus, ALP, and 25-OHD along with their respective standard deviations and ranges. It was discovered that patients with a lack of vit D had greater instances of hypocalcemia (28%) compared to those with vit D inadequacy (24.7%), Yet it was not determined that it was statistically meaningful (p-value = 0.885, Table II). 38 patients (39%) had increased ALP, 38 (98.3%) required insufficient vit D, and one (3.7%) had sufficient vit D. The serum level of ALP was normal in 63 (or 63%) of the patients (p 0.001, Table III).

Table 1. Value and Prevalence of a Biochemical Component

Biochemical Parameter	Value		Frequency	
	Mean + SD	Range		
Serum phosphorus, mmol/L	2.34 + 0.38	0.98 - 2.8	Normal	97 (97%)
			Low	5 (5%)
Serum calcium, mmol/L	3.4 + 0.256	2.99 - 3.86	Normal	75 (75%)
			Low	27 (27%
Vit D3, nmol/L	40 + 31	8.6 – 228	Normal	7 (7%)
			Insufficiency	23 (23%)
			Deficiency	73 (73%)
Serum ALP, U/L	310.06 +276.	64 236 – 2131	Normal	63 (63%)
			High	39 (39%)

Table 2. Comparing the amounts of Vitamin D3 and Serum Calcium Phosphorous in the Blood.

Serum Level						
	Calcium		p-value	Phosphorous		p-value
Vitamin D3	Low	Normal		Low	Normal	
	n (%)	n (%)		n (%)	N (%)	
Normal Vitamin D	2 (33.33)	4 (66.67)		2 (17.78)	6 (94.44)	
Inadequacy Vitamin D	5 (22.77)	17 (77.23)	0.974	1 (1)	23 (100)	0.29
Deficit Vitamin D	19 (26.38)	53 (73.61)		4 (5.28)	70 (95.83)	

Table 3. Serum vit D and Alkaline Phosphatase Comparison.

Serum vitamin D3	Serum Alkaline Phosphatse		p-value
	Normal n (%)	High n (%)	
Normal Vitamin D	6 (100%)	0 (0%)	0.002
Inadequacy Vitamin D	21 (95.45%)	1 (4.55%)	
Deficit Vitamin D	35 (48.61%)	37 (51.39%)	

Discussion

Several studies have connected hypovitaminosis D in else the aged and fit adults to non-specific musculoskeletal pain. GP may be a particular symptom of children's vit D insufficiency. It was discovered that 72% of the youngsters with GP were vit D deficient and 94% of them had hypovitaminosis D. In the study population, there was found to be a low dietary intake of calcium, which can be found in milk and other dairy

products. Only 17% of the kids drank milk that had been fortified with vit D. (Li 2022).

Research suggests that low vit D levels and growing discomfort can be related. GP was once thought to be a sign of calcium deficiency, according to Abraham Jacobi. According to research, there may be a connection between low vit D levels and the development of pain. According to Abraham Jacobi, GP was long thought to be a symptom of a calcium deficiency. He also suggested a link between the aetiology of GP and adult nighttime cramps brought on by a calcium deficiency (Liao 2020).

GP has recently been connected by some sources of vit D and calcium deficiencies. GP is simply a clinical manifestation of hypovitaminosis D, based on a blog post by James Dowd about vit D. Just 26% of the participants in this study exhibited hypocalcemia (Naiboglu 2020).

Contrary to data, which indicated that 46% of patients with hypovitaminosis D had low serum calcium levels. Their research population comprised participants who were sent to them with aberrant regular biochemistry and musculoskeletal issues, which led to the observation of this disparity. Nearly similar to the 81% of kids described by Peacey who already had normal serum PO values, 97% of the children had normal blood PO levels. Despite the fact that 51.39% of our participants had higher serum ALP concentrations due to Vit D deficiency, a lack of vit D was not found to be linked to increased ALP levels. These results corroborate those of an Iranian investigation that highlights the inadequate sensitivity of typical biochemical indicators (ALP, PO, and Ca) to detect vit D insufficiency (Pavone 2019, Russell 2021).

At minimum one biochemical sign had a specificity of 24.2%, 13.8%, and 6% to identify acute, moderate, and minor vit D deficiency, correspondingly. 20 Some researchers have discovered that common biochemical markers of bone resorption are erroneous, even in the context of secondary hyperparathyroidism.

Serum calcium, PO, and ALP are examples of bone turnover markers that are typically suggested by doctors and are thought to be indicative of bone homeostasis. However, only a small percentage of individuals (6%), and hypophosphatemia (3%), were found to have these conditions in this study. About 38% of patients had high ALP levels. Serum ALP concentration alone was employed in a previous study as a marker of bone health in Kashmiri children with limb complaints.

According to the study, people with hypovitaminosis D may have serum levels of common markers of bone turnover that are normal, and Such markers by themselves, without serum levels of PTH and 25-OHD are not accurate predictors of bone state. The majority of people with hypovitaminosis D are likely to go undetected if routine biochemical markers are utilized alone.

Decreased serum levels of 25-OHD combined with secondary hyperparathyroidism result in osteopenia and lower bone mineral content. It is generally acknowledged that those who have lower bone mineral content when they are young and just before puberty are more likely to suffer osteopenic fractures later in life.(2) To determine whether kids with hypovitaminosis D who are experiencing developmental pain are much more likely to have a poor density of bone minerals and an increased probability of fractures in the long term, more research is required.

Conclusion

Otherwise healthy children with growing and unexplained limb pains should be assessed for Vit D Deficiency and treated.

References

Ahmed, N., Ahmed, K. A., Siddique, T., Ahmed, R. I., Aftab, M., & Bibi, R. (2022). Vitamin D Deficiency in Children/Adolescent Presenting with Night Time Legs Pain. *Pakistan Journal of Medical & Health Sciences. 16*(04), 1003. https://doi.org/10.53350/pjmhs221641003

Ali, M. A., Haque, M., Islam, M. I., Khan. M. Z. I., Rahman, S. A. (2022). Serum Vitamin D and Bone Mineral Density in Children with Growing Pain in a Tertiary Hospital of Bangladesh. *Open Journal of Pediatrics. 12*(5), 815-26. https://doi.org/10.4236/ojped.2022.125082

Bughio, R., Ahmed, A., Ashfaq, M., Nisa, B. U., Hussain, W. (2020). Vitamin D Deficiency in Children with and without Cystic Fibrosis: A Cross-Sectional Study. *Journal of the Dow University of Health Sciences (JDUHS). 14*(3), 114-8. https://doi.org/10.36570/jduhs.2020.3.1007

Čulić, S. (2021). Viral Infections, Including Influenza and Corona Virus Disease 2019, and Vitamin D: A Mini-Review. Vitamin D. https://doi.org/10.5772/intechopen.96102

Dijkstra, J. N., Boon, E., Kruijt, N., Brusse, E., Ramdas, S., & Jungbluth, H. (2023). Muscle cramps and contractures: causes and treatment. *Practical Neurology. 23*(1), 23-34. http://dx.doi.org/10.1136/pn-2022-003574

Fernandes, M. A., Melo, I., Costa, F. C., & Salgado, M. (2019). Definition and characterization of muskoloskeletal pain and associated diseases. *Nascer E Crescer-Birth and Growth Medical Journal. 28*(4), 203-15. https://doi.org/10.25753/BirthGrowthMJ.v28.i4.15457

Habib, A. M., Nagi, K., Thillaiappan, N. B., Sukumaran, V., & Akhtar, S. (2020). Vitamin D and its potential interplay with pain signaling pathways. *Frontiers in immunology. 11*, 820. https://doi.org/10.3389/fimmu.2020.00820

Huang, H., & Cao, Y. (2022). The Development of Rickets in Children and Nursing Contributions to Treatment. *Alternative Therapies in Health and Medicine. 28*(1), 86-91.

Jeyakumar, A., & Shinde, V. (2019). A systematic review and meta-analysis of the prevalence of vitamin D deficiency among adolescent girls in selected Indian states. *Nutrition and health. 25*(1), 61-70. https://doi.org/10.1177/0260106018805360

Kanta, P., & Gopinathan, N. R. (2019). Idiopathic growing pains in pediatric patients: a review of the literature. *Clinical Pediatrics. 58*(1), 5-9. https://doi.org/10.1177/0009922818784956

Karim, R., Afridi, J. K., Ullah, H., Zaman, M. B., Amjad, A., Naeem, S. (2022). Hypovitaminosis D Causing Idiopathic Musculoskeletal Pain in Children. *Journal of Gandhara Medical and Dental Science, 9*(4), 58-62. https://doi.org/10.37762/jgmds.9-4.323

Li, H., Wang, B., He, L., Tao, R., & Shang, S. (2022). Application of bone metabolic parameters in the diagnosis of growing pains. *Journal of Clinical Laboratory Analysis. 36*(2), 24184. https://doi.org/10.1002/jcla.24184

Liao C-Y, Wang L-C, Lee J-H, Wu K-W, Lin Y-T, Yang Y-H, (2022). Clinical, laboratory characteristics and growth outcomes of children with growing pains. *Scientific Reports. 12*(1), 14835. https://doi.org/10.1038/s41598-022-19285-3

Naiboglu, S., Naiboglu, E., Sayman, O. A., & Demirkan, F. G. (2020). Retrospective Evaluation of Pediatric Patients with Extremity Pains/Ekstremite Agrisi ile Cocuk Poliklinigine Basvuran Cocuk Hastalarin Retrospektif Degerlendirilmesi. *Bagcilar Medical Bulletin. 5*(2), 40-50. https://doi.org/10.4274/BMB.galenos.2020.03.10

Pavone, V., Vescio, A., Valenti, F., Sapienza, M., Sessa, G., & Testa, G. (2019). Growing pains: What do we know about etiology? A systematic review. *World Journal of*

Orthopedics. 10(4), 192. https://doi.org/10.5312/wjo.v10.i4.192

Russell, C. (2021). Benign nocturnal idiopathic leg pain: A qualitative study of experiences of New Zealand caregivers. https://hdl.handle.net/10652/5490