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Correlation of Serum Vitamin D3 Levels with Febrile Seizures in Children Aged 6 Months to 5 Years: A Cross-Sectional Study

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Abstract

Febrile seizures are the most common convulsive disorder of early childhood. Emerging evidence implicates vitamin D deficiency in neuronal hyperexcitability, raising interest in its association with febrile seizures. This hospital-based cross-sectional study enrolled 65 children aged 6 months to 5 years admitted with febrile seizures at Kempegowda Institute of Medical Sciences (KIMS), Bangalore, over 18 months. Serum 1,25-dihydroxycholecalciferol (vitamin D3) levels were measured and categorised using IAP 2017 guidelines: deficient (<12 ng/mL), insufficient (12–20 ng/mL), and sufficient (>20 ng/mL). Demographic, clinical, hematological, and biochemical parameters were recorded and analysed. Vitamin D deficiency was present in 11 children (16.9%) and insufficiency in 38 (58.5%), with only 16 (24.6%) having sufficient levels, yielding a hypovitaminosis D prevalence of 75.4%. Mean serum vitamin D was 16.41 ± 6.58 ng/mL. Male predominance was noted (63.1%; ratio 1.7:1), with peak incidence in the 2–3-year age group (33.8%). Most children experienced a single convulsion (69.2%), and seizures occurred predominantly within the first two days of fever. A

statistically significant association was found between vitamin D status and number of convulsions (Fisher's Exact Test, p = 0.03): children with vitamin D deficiency had a higher proportion of multiple convulsions. Anemia was prevalent (55.4%) and also significantly associated with seizure frequency (p = 0.015). No significant associations were found between inflammatory markers (CRP, ESR, TLC) and vitamin D levels. On three-month follow-up with vitamin D3 supplementation, only 1 of 65 children experienced seizure recurrence. Vitamin D insufficiency is highly prevalent among children with febrile seizures and correlates significantly with seizure frequency, supporting a role for routine vitamin D assessment and supplementation in this population.

Keywords: Febrile seizures, Vitamin D deficiency, Paediatric seizures, Serum 25(OH)D, Anemia, Neuronal excitability, Children, Nutritional deficiency, Seizure recurrence, IAP guidelines

Introduction

Febrile seizures are convulsions occurring in young children between 6 months and 5 years of age in association with fever, in the absence of central nervous system (CNS) infection or metabolic abnormalities. They represent the most common seizure disorder of early childhood, affecting 2–5% of children globally, with higher rates of up to 12% reported in specific populations [1]. The peak incidence occurs in the second year of life, and approximately one-third of affected children experience at least one recurrence. Despite their generally benign prognosis, febrile seizures cause significant parental anxiety and contribute substantially to emergency department visits and paediatric admissions [2].

The neurobiological basis involves an interaction between fever-driven increase in neuronal excitability, the intrinsic vulnerability of the immature brain, and pro-inflammatory cytokines released during systemic infection. The relative immaturity of GABAergic inhibitory circuits and the dominance of excitatory glutamatergic signalling in early childhood predispose the developing brain to seizure generation under febrile conditions [3].

Vitamin D is increasingly recognised as a neuroactive steroid with roles extending well beyond skeletal metabolism. Vitamin D receptors (VDR) are widely expressed in the brain, including in cortical neurons, hippocampus, substantia nigra, and glial cells. Active vitamin D (calcitriol) influences neuronal differentiation, calcium homeostasis, antioxidant pathways, and regulation of pro-inflammatory cytokines – all mechanisms relevant to seizure susceptibility [4,5]. Vitamin D deficiency is pandemic among children worldwide, including in sun-rich countries such as India, driven by indoor lifestyles, dietary inadequacy, and limited supplementation [6].

Several observational studies have reported lower serum 25-hydroxyvitamin D (25(OH)D) levels in children with febrile seizures compared with febrile controls, and some have demonstrated a negative correlation between vitamin D concentrations and seizure recurrence [7,8]. However, findings are inconsistent across populations [9], and published Indian data remain limited. This study was therefore undertaken to determine the prevalence of vitamin D deficiency among children presenting with febrile seizures at a tertiary centre in Bangalore, and to analyse its association with seizure frequency and other laboratory parameters.

Materials And Methods

Study Design and Setting

A hospital-based cross-sectional observational study was conducted at the Department of Paediatrics, KIMS and Research Centre, Bangalore, over a period of 18 months (2023–2026). Institutional Ethics Committee approval was obtained, and written informed consent was taken from parents or legal guardians of all participants.

Participants

Children aged 6 to 60 months admitted with febrile seizures were included. Exclusion criteria were: afebrile seizures, clinical or laboratory evidence of CNS infection, structural CNS malformations, and chronic systemic illness. Based on a prevalence estimate of 13.5% (Singh et al., 2019) and 10% precision, the calculated minimum sample size was 45; 65 consecutive eligible children were enrolled.

Data Collection

Detailed demographic and clinical information was recorded using a structured proforma. Physical examination included anthropometric assessment classified according to the Indian Academy of Pediatrics (IAP) nutritional grading. Laboratory investigations included complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum electrolytes (sodium, potassium, chloride, calcium), random blood glucose (GRBS), and urine routine examination.

Vitamin D Measurement

Five millilitres of venous blood were collected from each child. Serum 25-hydroxyvitamin D3 was measured using a 25-hydroxy vitamin D3 EIA kit on an immunoassay analyser. Vitamin D status was categorised per IAP 2017 guidelines: sufficient (>20 ng/mL), insufficient (12–19 ng/mL), and deficient (<12 ng/mL). All children with low or insufficient vitamin D were started on vitamin D3 supplementation and followed up at three months to assess seizure recurrence.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using standard statistical software. Descriptive statistics (mean, standard deviation, frequency, and percentage) summarised continuous and categorical variables. Associations between categorical variables were evaluated using the chi-square test or Fisher's Exact Test as appropriate. A p-value <0.05 was considered statistically significant.

Results and Discussion

Demographic and Clinical Profile

Among 65 children enrolled, the most common age group was 2–3 years (33.8%), followed by 1–2 years (29.2%), 4–5 years (16.9%), 6–12 months (13.8%), and 3–4 years (6.2%), with a mean age of 25.02 ± 14.75 months (Table 1). This clustering in the second and third years of life reflects the well-established epidemiological pattern of febrile seizures and corresponds to the peak period of neurological vulnerability [1,2]. Comparable age distributions were reported by Heydarian et al. (2020) from Iran and Gowdaman et al. (2024) from Vellore [9,10].

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 65)

Parameter	Category	n (%)	p-value
Age group (months)	6–11	9 (13.8%)	
	12–23	19 (29.2%)	

Parameter	Category	n (%)	p-value
	24–35	22 (33.8%)	
	36–47	4 (6.2%)	
	48–60	11 (16.9%)	$\chi^2 = 7.23$, $p = 0.51$
Gender	Male	41 (63.1%)	
	Female	24 (36.9%)	M:F = 1.7:1
Temperature (°F)	99–100	17 (26.2%)	
	100–101	30 (46.2%)	
	>101	18 (27.7%)	Mean 100.72 ± 0.8
Fever duration (days)	1	29 (44.6%)	
	2	27 (41.5%)	Mean 1.76 ± 0.93
No. of convulsions	1	46 (69.2%)	
	2	18 (27.7%)	
	4	1 (1.5%)	Mean 1.47 ± 0.45
Past H/o febrile seizure	Absent	64 (98.5%)	
	Present	1 (1.5%)	
Immunisation status	Age-appropriate	65 (100%)	
Nutritional status (IAP)	Normal	39 (60.0%)	
	Grade I undernutrition	16 (24.6%)	
	Grade II undernutrition	8 (12.3%)	
	Grade III/IV undernutrition	2 (3.1%)	

Male predominance (63.1%; M: F ratio 1.7:1) is consistent with multiple published series including Hossain et al. (2023) from Dhaka (54.5% male) [7] and Zhang et al. (2024) from China (M: F 1.43:1) [11]. The biological basis for this predisposition remains incompletely understood but may reflect sex-linked differences in neuronal maturation and seizure threshold.

Moderate-grade fever (100–101°F) was the most common temperature category (46.2%), with mean temperature 100.72 ± 0.8°F, underscoring that febrile seizures occur across a broad thermal range rather than exclusively at high temperatures. Seizures occurred predominantly within the first two days of illness (44.6% on day 1; 41.5% on day 2), consistent with the

established pattern of early seizure onset during febrile illness [12]. The vast majority of children (69.2%) experienced a single convulsion, consistent with simple febrile seizures. All children were appropriately immunised and developmentally normal, excluding these as contributing factors.

Hematological Parameters and Anemia

Mean hemoglobin was 10.64 ± 1.58 g/dL, indicating mild anemia at the cohort level. Fifty-five point four percent of children were anemic: 16.9% had mild anemia (10–10.9 g/dL) and 38.5% had moderate anemia (6–9.9 g/dL) (Table 2). A statistically significant association was found between hemoglobin level and number of convulsions (Fisher's Exact Test, p = 0.015): among children with hemoglobin 6–9.9 g/dL, 52% experienced two convulsions compared with only 13.8% of those with hemoglobin ≥11 g/dL.

Table 2: Association between Hemoglobin Level and Number of Convulsions (n = 65)

Hemoglobin (g/dL)	1 Convulsion n (%)	2 Convulsions n (%)	4 Convulsions n (%)
≥11 (Normal)	25 (86.2%)	4 (13.8%)	0 (0%)
10–10.9 (Mild anemia)	10 (90.9%)	1 (9.1%)	0 (0%)
6–9.9 (Moderate anemia)	11 (44.0%)	13 (52.0%)	1 (4.0%)
Total	46 (70.8%)	18 (27.7%)	1 (1.5%)
Fisher's Exact Test	p = 0.015		

This finding is clinically significant. Iron deficiency anemia reduces oxygen delivery to the brain and may compromise inhibitory neuronal function. Namakin et al. (2016) similarly reported that iron and zinc deficiencies were associated with reduced inhibitory neurotransmission in febrile seizure children [13]. Papež et al. (2023), in a prospective multivariate study, identified iron status among the key predictors of febrile seizure risk and recurrence [14]. Our data corroborate these findings and suggest anemia as a potentially modifiable contributor to seizure burden.

Biochemical Parameters

Mean CRP was 1.45 ± 2.7 mg/dL, reflecting a mild inflammatory response. Mean serum sodium showed mild hyponatremia (134.89 ± 2.7 mEq/L), while potassium, chloride, and glucose were within normal limits. Serum calcium showed a statistically significant age-wise difference (p = 0.041), with the lowest mean in the youngest age group (8.59 mg/dL in 6–11 months), though values remained within normal clinical ranges. This gradient is clinically relevant given calcium's role in maintaining neuronal membrane potential; low vitamin D could further impair calcium homeostasis and lower seizure threshold, as proposed by Heydarian et al. (2020) and Al-Ashou et al. (2025) [9,15].

Vitamin D Status

The prevalence of hypovitaminosis D was high: 11 children (16.9%) were vitamin D deficient and 38 (58.5%) were insufficient, while only 16 (24.6%) had sufficient levels (Table 3). The mean serum vitamin D was 16.41 ± 6.58 ng/mL, in the insufficiency range. Vitamin D status was not significantly associated with age ($\chi^2 = 6.48$, p = 0.44) or gender (Fisher's Exact Test, p = 0.52), indicating that hypovitaminosis D was a

generalised characteristic of this cohort rather than confined to any demographic subgroup.

Table 3: Vitamin D Status in Study Participants (n = 65)

Vitamin D Category	Criteria (ng/mL)	n	Percentage (%)
Deficient	<12	11	16.9%
Insufficient	12–20	38	58.5%
Sufficient	>20	16	24.6%
Total		65	100%

These findings align closely with comparable Indian and international series. Gowdaman et al. (2024) from a tertiary centre in South India reported insufficiency and deficiency in 71% and 13% of febrile seizure children, respectively [10]. Singh et al. (2019) from Jammu and Kashmir found a strong association between low vitamin D and simple febrile seizures ($p < 0.01$) [16]. Zhang et al. (2024) from China demonstrated significantly lower median vitamin D in children with febrile seizures vs. healthy controls (28.8 vs. 37.51 ng/mL, $p < 0.05$) in a large cohort of 747 cases [11]. Çığrı et al. (2023) reported significantly lower vitamin D alongside selenium, zinc, and vitamin B12 in febrile seizure children compared with febrile controls ($p < 0.001$) [17]. In contrast, Mohammadi et al. (2023) and Heydarian et al. (2020) did not find statistically significant mean vitamin D differences between groups [9,18], highlighting that sample size, geographical variation, and seasonal factors may modulate results.

Association between Vitamin D Status and Seizure Frequency

The most important finding of this study was the statistically significant association between vitamin D status and number of convulsions (Fisher's Exact Test, $p = 0.03$) (Table 4). Among children with a single convulsion, only 8.7% were deficient and 56.5% insufficient; among those with two convulsions, 33.3% were deficient and 55.5% insufficient. The sole child with four convulsions was in the deficient category. Children with sufficient vitamin D were substantially less likely to have multiple convulsions.

Table 4: Association between Vitamin D Status and Number of Convulsions (n = 65)

No. of Convulsions	Deficient n (%)	Insufficient n (%)	Sufficient n (%)
1	4 (8.7%)	26 (56.5%)	14 (30.4%)
2	6 (33.3%)	10 (55.5%)	2 (11.1%)
4	1 (100%)	0 (0%)	0 (0%)
Total	11 (16.9%)	38 (58.5%)	16 (24.6%)
Fisher's Exact Test	p = 0.03		

This association is mechanistically plausible. Vitamin D modulates neuronal excitability through multiple pathways: regulation of L-type calcium channel expression, attenuation of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) known to lower seizure threshold, and upregulation of neurotrophic factors that stabilise synaptic networks [4,5]. In animal models, vitamin D pretreatment delays seizure onset and reduces severity in chemically induced paradigms; knockout of VDR leads to heightened seizure susceptibility [3,19]. Clinically, Bhat et al. (2020) demonstrated a significant negative correlation between 25(OH)D levels and seizure recurrence in 223 children with simple febrile seizures[8], a finding closely mirrored by our results. Hossain et al. (2023)7 and Nasir et al. (2024) [20] from South Asia similarly established significant associations between vitamin D deficiency and febrile seizure occurrence.

No significant associations were identified between vitamin D levels and inflammatory markers: CRP (p = 0.64), ESR (p = 0.82), or total leukocyte count (p = 0.73). This suggests that vitamin D's influence on seizure susceptibility operates through neuromodulatory and calcium-regulatory pathways rather than through gross systemic inflammation, supporting the view that vitamin D deficiency and inflammatory response represent distinct but potentially additive pathways in febrile seizure pathogenesis [11,18].

Follow-Up Outcome

All 65 children were initiated on vitamin D3 supplementation following the index event and followed up at three months. Only 1 child (1.5%) experienced a recurrent febrile seizure during this period, suggesting a favourable short-term outcome with supplementation. Although this study was not a controlled trial and definitive conclusions on the preventive efficacy of supplementation cannot be drawn, these findings are consistent with prospective evidence from Bhat et al. (2020) and Gowdaman et al. (2024) suggesting that correcting vitamin D deficiency may attenuate recurrence risk [8,10]. Larger randomised controlled trials with adequate power and standardised supplementation protocols are needed to confirm this effect.

Conclusions

Vitamin D insufficiency and deficiency are highly prevalent (75.4%) among children aged 6 months to 5 years presenting with febrile seizures in this cohort. A significant association between lower vitamin D status and higher seizure frequency (p = 0.03) supports a neuromodulatory role for vitamin D in febrile seizure susceptibility. Anemia, present in 55.4% of children, was independently associated with increased convulsion frequency (p = 0.015). These micronutrient deficiencies represent potentially modifiable risk factors. Clinicians should consider routine assessment of serum vitamin D and hemoglobin in children with febrile seizures, particularly with recurrent episodes during the same illness. Supplementation of vitamin D3, alongside dietary counselling, promotion of outdoor sun exposure, and correction of iron-deficiency anemia, should be integrated into standard febrile seizure management protocols and national child health programmes. Prospective randomised trials are warranted to establish optimal supplementation regimens and confirm their preventive efficacy.

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References

1. Xixis KL, Samanta D, Smith T, Keenaghan M. Febrile seizure. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
2. Leung AK, Hon KL, Leung TN. Febrile seizures: an overview. Drugs Context. 2018; 7:212536.
3. Mosili P, Maikoo S, Mabandla M, Qulu L. The pathogenesis of fever-induced febrile seizures and its current state. Neurosci Insights. 2020;15: 2633105520956973.
4. Cui X, Eyles DW. Vitamin D and the central nervous system: causative and preventative mechanisms in brain disorders. Nutrients. 2022; 14(20):4353.
5. Sailike B, Onzhanova Z, Akbay B, Tokay T, Molnár F. Vitamin D in central nervous system: implications for neurological disorders. Int J Mol Sci. 2024;25(14):7809.
6. Oktaria V, Putri DAD, Ihyauddin Z, Julia M, Sulistyoningrum DC, Koon PB, et al. Vitamin D deficiency in South-East Asian children: a systematic review. Arch Dis Child. 2022;107 (11):980–7.
7. Hossain MI, Khanam W, Adnan MA, Mawa J, Ahmed I, Mondol MT. Association of serum vitamin D levels and simple febrile seizures in children. Int J Contemp Pediatr. 2023; 10:266–71.
8. Bhat JA, Bhat TA, Sheikh SA, Wani ZA, Ara R. Status of 25-hydroxy vitamin D level in simple febrile seizures and its correlation with recurrence of seizures. Asian J Med. 2020;10(01):6–9.
9. Heydarian F, Bakhtiari E, Golmakani H, Ghasemi NF, Heidarian M. Serum level of vitamin D and febrile seizure: a clinical study. Iran J Child Neurol. 2020;14(3):77.
10. Gowdaman K, Ahmed MS, Sreedharan M, Pillai MCM, Venkatesh G. Role of vitamin D deficiency in pediatric febrile seizures. Res J Med Sci. 2024; 19:154–60.
11. Zhang L, Lin X, Liu B, Liu Q. Clinical characteristics and serum 25-hydroxyvitamin D levels in children with febrile seizures in China. Sci Rep. 2024;14(1):23330.
12. Thadchanamoorthy V, Dayasiri K. Review on febrile seizures in children. Int Neuropsychiatr Dis J. 2020; 12:25–35.
13. Namakin K, Zardast M, Sharifzadeh G, Bidar T, Zargarian S. Serum trace elements in febrile seizure: a case-control study. Iran J Child Neurol. 2016;10(3):57.
14. Papež J, Labounek R, Jabandžiev P, Česká K, Slabá K, Ošlejšková H, et al. Multivariate linear mixture models for the prediction of febrile seizure risk and recurrence: a prospective case-control study. Sci Rep. 2023;13(1):17372.
15. Al-Ashou S, Alashou O, Azeez Y. The association of serum vitamin D and calcium level with febrile convulsions. Res Med Biol. 2025;16(2):e25066.
16. Singh V, Sharma P, Dewan D. Association of vitamin D levels with simple febrile seizures in under five children: a case-control study. 2019.
17. Çığrı E, İnan FÇ. Comparison of serum selenium, homocysteine, zinc, and vitamin D levels in febrile children with and without febrile seizures: a prospective single-center study. Children. 2023;10(3):528.
18. Mohammadi M, Baleghi Y, Salehiomran M, Hajiahmadi M, Poornasrollah M, Alijanpour P, et al. Evaluation of vitamin D level in children with febrile seizure referred to Amirkola Children's

Hospital, Babol. Global Pediatr Health. 2023; 10:2333794X231198390.

19. Pendo K, DeGiorgio CM. Vitamin D3 for the treatment of epilepsy: basic mechanisms, animal models, and clinical trials. Front Neurol. 2016; 7:218.
20. Nasir F, Shakoor I, Iqbal SA, Masood S, Farrukh R, Naseer A. Paediatric patients-based case-control analysis: the association between serum vitamin D levels and febrile seizures. Pak Armed Forces Med J. 2024;74(2):335.