Original Article

Clinical and Biochemical Predictors of Hypocalcemic Seizures in Infancy: Association with Age, Gender, Breastfeeding, and Growth Parameters

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Abstract

Background: Early recognition of clinical and biochemical predictors may help identify high-risk infants and allow timely correction of calcium imbalance. The objective is to evaluate the clinical and biochemical predictors of hypocalcemic seizures in infancy, with emphasis on age, gender, breastfeeding status, growth parameters, and corrected calcium levels. **Material and Methods:** This prospective observational study included 100 infants aged 1 month to 2 years presenting with seizures to the Department of Pediatrics, Kodagu Institute of Medical Sciences, Madikeri. Infants with central nervous system infection, congenital brain malformations, and maternal drug or supplement exposure affecting bone mineral metabolism were excluded. Corrected calcium was calculated, and hypocalcemia was defined as corrected serum calcium <8 mg/dL. **Results:** Among 100 infants, 27 (27.0%) had hypocalcemic seizures and 73 (73.0%) had non-hypocalcemic seizures. Hypocalcemia was significantly more common in infants aged <6 months, affecting 20 of 49 infants (40.8%), compared with 4 of 25 (16.0%) infants aged 6 months to 1 year and 3 of 26 (11.5%) infants aged 1–2 years ($p = 0.009$). Female infants showed a significantly higher frequency of hypocalcemia than males, 24 of 67 (35.8%) versus 3 of 33 (9.1%) ($p = 0.005$). All 27 infants with hypocalcemic seizures were breastfed. Length percentile was also significantly associated with hypocalcemia, with higher frequency among infants below the 50th percentile ($p = 0.002$). **Conclusion:** Hypocalcemic seizures in infancy were significantly associated with age <6 months, female gender, breastfeeding status, lower length percentile, and reduced corrected calcium levels.

Keywords: Hypocalcemic seizures; Infancy; Corrected serum calcium; Breastfeeding; Clinical predictors; Pediatric seizures.

Received: 05 May 2026 **Revised: 25 May 2026** **Accepted: 13 June 2026** **Published: 25 June 2026**

Introduction

Hypocalcemic seizures are an important and reversible cause of seizures during infancy. Infancy is a period of rapid neurological and skeletal growth, and even minor disturbances in calcium metabolism can significantly affect neuromuscular excitability.[1] Calcium plays a central role in neuronal membrane stability, synaptic transmission, muscle contraction, and regulation of action potentials. When serum calcium falls below the normal range, the threshold for neuronal depolarization decreases, resulting in increased neuronal excitability and a higher risk of seizures.[2] Because hypocalcemia is treatable, early recognition is clinically important to prevent recurrent seizures, unnecessary anticonvulsant use, prolonged hospitalization, and avoidable investigations.[3] Seizures in infancy have multiple causes, including febrile convulsions, epilepsy, central nervous system infections, structural brain abnormalities, hypoglycemia, hypomagnesemia, hyponatremia, and hypocalcemia. Among these, metabolic and electrolyte disturbances are particularly important because they can be detected through simple laboratory testing and corrected rapidly.[4] Hypocalcemia may present with generalized tonic-clonic seizures, tonic seizures, focal seizures, jitteriness, irritability, tetany, or even status epilepticus. However, classical clinical signs of hypocalcemia such as Chvostek sign and Trousseau sign may be absent in many infants, making biochemical screening essential.[5]

Several clinical and biochemical factors may influence the risk of hypocalcemic seizures in infancy. Age is one of the most relevant predictors because younger infants, particularly those below 6 months, have high calcium requirements due to rapid growth and may depend heavily on maternal vitamin D stores and breast milk intake.[6] If maternal vitamin D status is poor or supplementation is inadequate, these infants may develop hypovitaminosis D and secondary hypocalcemia. Therefore, infants in the early months of life may be more vulnerable to hypocalcemic seizures than older infants. Gender differences have also been reported in some clinical datasets, although the biological explanation is not always clear.[7] Variations in feeding practices, nutritional status, growth patterns, healthcare-seeking behavior, and sociocultural factors may

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DOI:
10.21276/amit.2026.v13.i2.769

How to cite this article: Meghashree N, Shaziya S, Kushvanth KN. Clinical and Biochemical Predictors of Hypocalcemic Seizures in Infancy: Association with Age, Gender, Breastfeeding, and Growth Parameters. Acta Med Int. 2026;13(2):805-809.

influence the observed relationship between gender and hypocalcemic seizures. Identifying whether male or female infants are more commonly affected in a local population may help clinicians recognize at-risk groups and interpret seizure presentations more carefully.[8]

Breastfeeding is another important factor in calcium and vitamin D metabolism. Breastfeeding remains the ideal source of infant nutrition and provides major immunological and developmental benefits. However, breast milk contains relatively low vitamin D unless maternal vitamin D stores are adequate or supplementation is provided.[9] As a result, exclusively breastfed infants born to vitamin D-deficient mothers may be at increased risk of vitamin D deficiency, impaired calcium absorption, and hypocalcemic seizures.[10] Therefore, the association between breastfeeding and hypocalcemic seizures should not be interpreted as a negative effect of breastfeeding itself, but rather as a reflection of maternal-infant vitamin D status and supplementation practices. Growth parameters such as weight, length, and anthropometric percentiles may also provide useful clinical clues.[11] Poor growth, lower length percentile, or stunting may suggest chronic nutritional deficiency, vitamin D deficiency, or impaired mineral metabolism. Infants with lower length percentiles may have underlying nutritional compromise that increases susceptibility to hypocalcemia.[12]

Similarly, abnormal biochemical markers such as low corrected calcium, altered phosphorus, elevated alkaline phosphatase, and low vitamin D levels may support a diagnosis of metabolic bone disease or vitamin D deficiency-related hypocalcemia.[13] Corrected serum calcium is especially important in evaluating suspected hypocalcemic seizures because total calcium is affected by serum albumin concentration. A falsely low or misleading total calcium value may occur if albumin is abnormal. Correcting calcium for albumin provides a more clinically meaningful estimate of calcium status.[14] In infants presenting with seizures, especially those without evidence of infection, structural neurological disease, or developmental abnormality, corrected calcium estimation should be considered an essential part of the initial workup.[15]

Objective

To evaluate the clinical and biochemical predictors of hypocalcemic seizures in infancy, with emphasis on age, gender, breastfeeding status, growth parameters, and corrected calcium levels.

Materials and Methods

This was a prospective analytical study based on infants presenting with seizures. The study was conducted in the Department of Pediatrics, Kodagu Institute of Medical Sciences, Madikeri. A total of 100 infants aged 1 month to 2 years presenting with seizures were included. Infants from 1 month to 2 years of age presenting with seizures and otherwise developmentally normal infants were included. Infants with CNS infections such as meningitis, known congenital brain malformations, and infants whose mothers were receiving drugs or supplements known to affect bone mineral metabolism were excluded.

Data Collection: At admission, age, sex, demographic profile, clinical presentation, seizure type, seizure frequency, seizure duration, treatment received, past history of seizures, breastfeeding status, weight, length, head circumference, and biochemical findings were recorded in a predesigned proforma. The thesis notes that age, sex, demographic data, and clinical presentation were recorded at admission after written informed consent. Blood samples were collected under aseptic precautions and analyzed for serum calcium, albumin, corrected calcium, phosphorus, alkaline phosphatase, magnesium where available, and vitamin D where available. Corrected calcium was calculated as total calcium + 0.8 × (4 − serum albumin), and hypocalcemia was defined as corrected calcium <8 mg/dL. The major predictor variables included age group, sex, breastfeeding status, seizure type, weight percentile, length percentile, and corrected calcium level. The outcome variable was the presence or absence of hypocalcemic seizure.

Statistical Analysis: Data were tabulated using Microsoft Excel. Categorical variables were expressed as percentages. Chi-square test and Fisher's exact test were used to compare hypocalcemic and non-hypocalcemic groups. A p-value ≤0.05 was considered statistically significant.

Results

The association between age and hypocalcemic seizures was statistically significant. Among infants aged less than 6 months, 20 of 49 (40.8%) had hypocalcemia. In comparison, hypocalcemia was present in 4 of 25 (16.0%) infants aged 6 months to 1 year and 3 of 26 (11.5%) infants aged 1 to 2 years. This association was statistically significant with chi-square = 9.434 and p = 0.009, indicating that infants younger than 6 months were more prone to hypocalcemic seizures.

Table 1: Association of age group with hypocalcemic seizures

Age group	Hypocalcemia absent	Hypocalcemia present	Total	% with hypocalcemia	p-value
<6 months	29	20	49	40.8%	0.009*
6 months to 1 year	21	4	25	16.0%	
1 year to 2 years	23	3	26	11.5%	
Total	73	27	100	27.0%	

Gender was also significantly associated with hypocalcemic seizures. Among 33 male infants, only 3 (9.1%) had hypocalcemia, whereas among 67 female infants, 24 (35.8%) had hypocalcemia. The association was statistically significant with p = 0.005, suggesting a higher burden of hypocalcemic seizures among female infants in this study population.

Table 2: Association of gender with hypocalcemic seizures

Sex	Hypocalcemia absent	Hypocalcemia present	Total	% with hypocalcemia	p-value
Male	30	3	33	9.1%	0.005*
Female	43	24	67	35.8%	
Total	73	27	100	27.0%	

Breastfeeding showed a significant association with hypocalcemic seizures. All 27 infants with hypocalcemic seizures were breastfed. Among 86 breastfed infants, 27 developed hypocalcemia, whereas none of the 14 non-breastfed infants had hypocalcemia. This finding may reflect low maternal vitamin D stores and infant hypovitaminosis D rather than breastfeeding itself being causative.

Table 3: Association of breastfeeding with hypocalcemic seizures

Breastfed	Hypocalcemia absent	Hypocalcemia present	Total	% with hypocalcemia
Yes	59	27	86	31.4%
No	14	0	14	0.0%
Total	73	27	100	27.0%

Growth parameters were also examined. Weight percentile was not significantly associated with hypocalcemia, but length percentile showed a significant relationship. Hypocalcemia was seen in 1 of 2 (50.0%) infants below the 3rd length percentile, 21 of 48 (43.7%) infants between the 3rd and 50th percentile, and 5 of 45 (11.1%) infants between the 50th and 97th percentile. None of the infants above the 97th percentile had hypocalcemia. This association was statistically significant with p = 0.002.

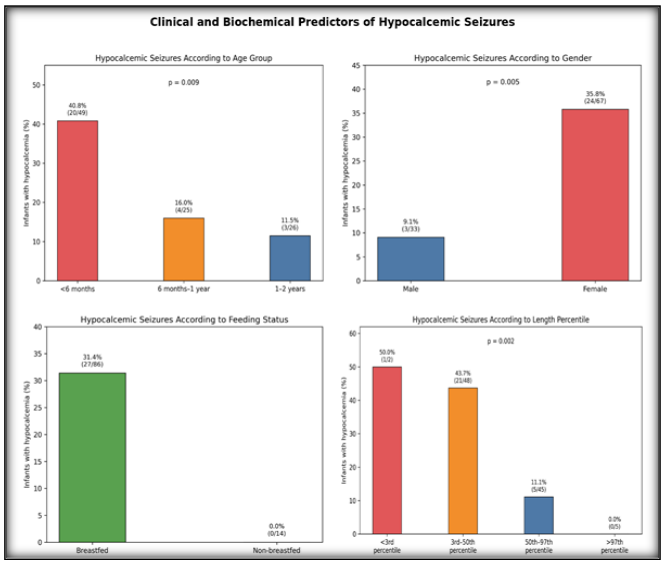
Table 4: Association of length percentile with hypocalcemic seizures

Length percentile	Hypocalcemia absent	Hypocalcemia present	Total	% with hypocalcemia	p-value
<3rd percentile	1	1	2	50.0%	0.002*
3rd–50th percentile	27	21	48	43.7%	
50th–97th percentile	40	5	45	11.1%	
>97th percentile	5	0	5	0.0%	
Total	73	27	100	27.0%	

Corrected calcium levels were strongly associated with hypocalcemic seizures. Among the 27 hypocalcemic infants, 1 (3.7%) had corrected calcium <4 mg/dL, 10 (37.0%) had corrected calcium between 4–6 mg/dL, and 16 (59.2%) had corrected calcium between 6–8 mg/dL. No infant with corrected calcium >8 mg/dL was classified as hypocalcemic.

Table 5: Distribution of corrected calcium levels among infants with hypocalcemic seizures

Corrected calcium level	Hypocalcemia absent	Hypocalcemia present	Total
<4 mg/dL	0	1	1
4–6 mg/dL	0	10	10
6–8 mg/dL	4	16	20
>8 mg/dL	69	0	69
Total	73	27	100



Discussion

The present study evaluated clinical and biochemical predictors associated with hypocalcemic seizures among infants aged 1 month to 2 years. The findings showed that hypocalcemic seizures were significantly associated with younger age, female gender, breastfeeding status, lower length percentile, and reduced corrected calcium levels. These results suggest that hypocalcemic seizures in infancy are not randomly distributed but are more likely to occur in infants with specific nutritional, developmental, and biochemical risk profiles. Age was one of the strongest clinical predictors of hypocalcemic seizures. Among infants younger than 6 months, 20 out of 49 (40.8%) had hypocalcemia, compared with 4 out of 25 (16.0%) infants aged 6 months to 1 year and 3 out of 26 (11.5%) infants aged 1 to 2 years. This association was statistically significant (p = 0.009), indicating that infants below 6 months were most vulnerable. This may be explained by the rapid skeletal growth and high calcium requirement during early infancy. Younger

infants are also more dependent on maternal vitamin D stores and early feeding practices, making them more susceptible to vitamin D deficiency-related hypocalcemia.[16]

Gender was also significantly associated with hypocalcemic seizures. Female infants showed a higher frequency of hypocalcemia, with 24 out of 67 (35.8%) affected, compared with only 3 out of 33 (9.1%) male infants ($p = 0.005$). Although the exact biological mechanism for this gender difference is not clear, it may reflect differences in nutritional exposure, health-seeking behavior, cultural feeding practices, or sample-specific variation. This finding should be interpreted carefully because gender-based susceptibility may vary across populations, but in this dataset, female gender was clearly associated with a higher burden of hypocalcemic seizures.[17] Breastfeeding was another important factor. All 27 infants with hypocalcemic seizures were breastfed. Among 86 breastfed infants, 27 (31.4%) developed hypocalcemia, whereas none of the 14 non-breastfed infants had hypocalcemia. This does not mean breastfeeding causes hypocalcemia. Breastfeeding remains the best and safest form of infant nutrition. The more likely explanation is that breastfed infants may become vitamin D deficient if maternal vitamin D levels are low or if infant vitamin D supplementation is not provided. Since breast milk naturally contains limited vitamin D, exclusively breastfed infants born to vitamin D-deficient mothers may be at greater risk of hypovitaminosis D, impaired calcium absorption, and hypocalcemic seizures.[18]

Growth parameters also showed an important relationship with hypocalcemic seizures. Weight percentile was not significantly associated with hypocalcemia, but length percentile showed a statistically significant association ($p = 0.002$). Hypocalcemia was present in 1 out of 2 (50.0%) infants below the 3rd length percentile and 21 out of 48 (43.7%) infants between the 3rd and 50th percentile, compared with only 5 out of 45 (11.1%) infants between the 50th and 97th percentile. No infant above the 97th percentile had hypocalcemia.[19] This suggests that lower length percentile or impaired linear growth may be linked with nutritional deficiency, chronic vitamin D insufficiency, or disturbed mineral metabolism. On a clinical level, these predictors can aid in the initial decision making process. In infants \(<\) 6 months, particularly those who are breastfed with LPs < 50, infants should be viewed as high-risk for hypocalcemic seizures. Serum calcium should be done early in the evaluation of such patients. If hypocalcemia is detected, check for possible vitamin D and magnesium deficiencies, as either can cause persistent or recurrent hypocalcemia. Early correction will help to avert further seizures and possibly decrease the need for unnecessary neuroimaging or lumbar puncture or extended anti-epileptic treatment. There are some limitations to this study. The number of infants in the sample was 100 from a single center and may restrict generalizability. Some associations may be dependent on local factors (e.g. gender, breastfeeding). Biochemical correlation was limited due to the fact that vitamin D and magnesium levels were not available for all infants. Follow-up for recurrence of seizures, neurodevelopmental outcomes and assessment of response to supplementation was not conducted over a longer period. Despite these drawbacks, the study is clinically significant and provides evidence that can be used in clinical practice because there are risk factors that are known to cause seizures with low calcium level.

Conclusion

This study demonstrated that certain clinical and biochemical factors, such as younger age, female gender, breastfeeding, lower length percentile, and lower corrected calcium levels are statistically significant predictors of hypocalcemic seizures in infancy. Hypocalcemia occurred more often in infants younger than 6 months and thus may be a critical time with regard to high growth and vitamin D and calcium requirements. In this study, female infants, and breastfed infants were more likely to develop hypocalcemic seizures, but breastfeeding was used here as an indirect measure of potential vitamin D deficiency rather than as a cause of seizures.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Chisti MJ, Salam MA, Ashraf H, Faruque AS, Bardhan PK, Shahid AS, Shahunja KM, Das SK, Ahmed T. Prevalence, clinical predictors, and outcome of hypocalcaemia in severely-malnourished under-five children admitted to an urban hospital in Bangladesh: a case-control study. J Health Popul Nutr. 2014 Jun;32(2):270-5. PMID: 25076664; PMCID: PMC4216963.
2. Hao, D., Wen, Z., & Jankovic, J. (2015). Genetics and molecular biology of brain calcification. Ageing Research Reviews, 22, 20–38. https://doi.org/10.1016/j.arr.2015.04.004
3. Gambardella, A., & Labate, A. (2014). The role of calcium channel mutations in human epilepsy. Progress in Brain Research, 213, 87–96. https://doi.org/10.1016/B978-0-444-63326-2.00004-1
4. Wang, G., et al. (2015). CaV3.2 calcium channels control NMDA receptor-mediated transmission: A new mechanism for absence epilepsy. Genes & Development, 29(14), 1535–1551. https://doi.org/10.1101/gad.260869.115
5. Teleanu, R. I., Sarman, M. A., Epure, D. A., Matei, M., Roşca, I., & Roza, E. (2023). Autosomal dominant hypocalcemia type 1 and neonatal focal seizures. Children, 10(6), 1011. https://doi.org/10.3390/children10061011
6. Abbasi, A. N., Ikram, F., Zaman, S., Nawaz, S. H., Hussain, S., & Shahid, H. (2023). Calcium and magnesium levels in children with febrile seizures admitted in a tertiary care hospital. Pakistan Armed Forces Medical Journal, 73(5), 1364.
7. Uzunhan, T. A., Kaçar, A., Mısırlı Özdemir, E. M., & Yapıcı, O. (2022). First afebrile seizures: Clinical and radiological view with emergent testing. Pediatrics International, 64(1), e15089. https://doi.org/10.1111/ped.15089
8. Tiwari, S., Adhikari, K. M., & Dhingra, S. (2021). Simple febrile seizures in toddlers: Do they have low serum calcium levels? Indian Journal of Child Health, 8(3), 119–121. https://doi.org/10.32677/IJCH.2021.v08.i03.003
9. Radi, A., Bakkali, O., Kmari, M., Ourrai, A., Hassani, A., Abilkassem, R., et al. (2020). Neonatal hypocalcemic seizures: About a 41-day-old infant. Asian Journal of Pediatric Research, 3(4), 9–14. https://doi.org/10.9734/ajpr/2020/v3i430133
10. Özçora, G. D. K. (2022). Evaluation of neurological prognosis in

children with hypocalcemic seizures due to vitamin D deficiency. Southern Clinics of Istanbul Eurasia, 33(4), 429–434. https://doi.org/10.14744/scie.2022.67299

11. Fayyaz, J., Rehman, A., Hamid, A., Khursheed, M., Zia, N., & Feroze, A. (2014). Age-related clinical manifestation of acute bacterial meningitis in children. Journal of Pakistan Medical Association, 64(3), 296.
12. Gowda, V. K., Kulhalli, J. P., Benakappa, S. N., & Benakappa, A. (2019). Etiological profile of afebrile seizures in infants in a tertiary care center from southern India. Journal of Pediatric Neurosciences, 14(2), 82. https://doi.org/10.4103/jpn.JPN_61_18\
13. Wagner CL, Greer FR. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. Pediatrics. 2008;122(5):1142-52. doi:10.1542/peds.2008-1862.
14. Institute of Medicine. Dietary reference intakes for calcium and vitamin D. Washington: National Academies Press; 2011. doi:10.17226/13050.
15. Pettifor JM. Nutritional rickets: deficiency of vitamin D, calcium, or both? Am J Clin Nutr. 2004;80(6 Suppl):1725S-9S. doi:10.1093/ajcn/80.6.1725S.
16. Kirkgoz T, Guran T. Primary adrenal insufficiency in children: diagnosis and management. Best Pract Res Clin Endocrinol Metab. 2018;32(4):397-424. doi:10.1016/j.beem.2018.05.010.
17. Asadullah, Shaikh S, Farhat A, Amanullah, Memon S, Chohan MN. Frequency of hypocalcaemia among children aged 2–60 months presenting with first episode of afebrile seizures: a cross-sectional study. J Pharm Res Int. 2021;33(60B):1063-8. doi:10.9734/jpri/2021/v33i60b34714.
18. Meesters K, Wassenberg T, Vanbesien J. Hypocalcemia as a cause of complex febrile seizures in a toddler. Case Rep Pediatr. 2021;2021:1798741. doi:10.1155/2021/1798741.
19. Hao D, Wen Z, Jankovic J. Genetics and molecular biology of brain calcification. Ageing Res Rev. 2015;22:20-38. doi:10.1016/j.arr.2015.04.004.