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Original Research Article

Spectrum of Etiologies of Hypocalcemic Seizures in Children Under Two Years of Age

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Abstract: *There are many causes of afebrile seizures, including metabolic disturbances; among them, hypocalcemia is the most common. Seizures related to hypocalcemia in infants are a serious clinical concern because they carry the risk of adverse long-term neurological and developmental outcomes.* ***Objective:*** *To determine the spectrum of etiologies of hypocalcemic seizures in children under two years of age.* ***Methods:*** *The current cross-sectional study was conducted at the neurology department of the children's hospital Faisalabad. The study duration was 8 months from June 2022 to February 2023. The overall sample size in our study was 54, calculated by using the WHO sample size calculator. Clinical information was collected from medical records, including key demographic and clinical details, such as age, sex, and seizure characteristics (type and frequency). Data were entered and analyzed using SPSS version 24.* ***Results:*** *A total of 54 patients with hypocalcemic fits were enrolled in the current study. Of 54 patients, males were 34 (62.96%) and females 20 (37.04%). Based on types of fits, generalized fits were observed in 42 (77.78%) patients, while focal fits were observed in 12 (22.22%) patients. The different causes of hypocalcemic fits were observed in our study: hypomagnesemia was the primary cause in 15 (27.78%) patients, followed by vitamin D deficiency in 11 (20.37%) patients, and hypoparathyroidism in 10 (18.52%) patients. In comparison, in only one patient (1.85%), the cause of hypocalcemia was pseudo-hypoparathyroidism.* ***Conclusion:*** *Our study concludes that hypomagnesemia, hypoparathyroidism, and vitamin D deficiency are the major causes of hypocalcemic fits. The findings highlight the importance of early detection, targeted nutritional interventions, and regular monitoring of calcium metabolism to reduce the risk of long-term complications.*

Keywords: Spectrum; Etiologies; Hypocalcemic Seizures; Children

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Introduction

Seizures are a common reason for visits to the pediatric emergency department and usually prompt a detailed evaluation to identify their causes. There are many causes of afebrile seizures, including metabolic disturbances; among them, hypocalcemia is the most common (1). Calcium plays a pivotal role in neurotransmitter release at synaptic membranes and at the neuromuscular junction, as well as in muscle contraction. Hypocalcemia decreases the threshold required for neuronal activation, thus increasing neuromuscular excitability (2). Seizures related to hypocalcemia in infants are a serious clinical concern because they carry the risk of adverse long-term neurological and developmental outcomes (3).

Hypoparathyroidism is an endocrine disorder caused by either inadequate production of parathyroid hormone (PTH) or resistance to its effects, which results in abnormal calcium and phosphorus balance in the body. In this condition, insufficient PTH leads to low serum calcium (hypocalcemia) and elevated serum phosphate (hyperphosphatemia), with corresponding abnormalities in measured PTH levels (4). The deficiency of PTH disrupts normal calcium and phosphorus homeostasis, increasing neuromuscular excitability and lowering the threshold for neuronal firing, which may contribute to the development of seizures (5). Chronic disturbances in calcium and phosphate metabolism are also associated with intracranial calcifications, particularly in the basal ganglia and other brain regions, which are recognized long-term sequelae in many patients with hypoparathyroidism (6). These calcifications are thought to arise from prolonged hyperphosphatemia and ectopic mineral deposition. Persistent hypocalcemia further enhances neuronal excitability and may increase susceptibility to epileptic activity and other neurological dysfunctions (7).

In recent years, metabolic abnormalities have increasingly been recognized as essential triggers of seizures, especially in infants and young toddlers. Among various biochemical disturbances, hypocalcemia is one of the most commonly reported metabolic causes associated with seizure activity in this age group (8, 10). Low serum calcium levels can enhance neuromuscular irritability and may precipitate seizures that are difficult to control with standard anticonvulsant therapy. Several clinical studies have highlighted the significant role of hypocalcemia in new-onset seizures in children without fever, often occurring at a moderate to high frequency. In a study conducted in Pakistan, more than two-thirds of children presenting with their first episode of afebrile convulsions were found to have hypocalcemia, raising concerns about the impact of nutritional deficiencies and low dietary calcium intake in lower-middle-income settings (11, 13).

Despite the clinical significance of the association between hypocalcemia and afebrile seizures, there is a lack of local data on this issue, particularly in countries such as Pakistan. Nutritional deficiencies, limited access to fortified foods, and suboptimal health practices in young children may increase the risk of calcium deficiency in infants. Understanding the prevalence of hypocalcemia in this population would help prioritize further investigations, enable timely correction of biochemical imbalances, and potentially reduce the need for more invasive, costly, or complex diagnostic procedures such as neuroimaging. Therefore, the present study was conducted to determine the frequency of causes of hypocalcemia in children less than two years of age presenting with afebrile seizures. The results are intended to inform clinical decision-making and contribute to the evidence base for improving pediatric seizure management in resource-limited settings.

Methodology

The current cross-sectional study was conducted in the neurology department of the Children's Hospital, Faisalabad. The study duration was 8 months from June 2022 to February 2023. The overall sample size in our study was 54, calculated by using the WHO sample size calculator. The hospital's ethics committee approved the study. The inclusion criteria of our study were all the infants of both genders and ages from two months to two years with seizures, who were admitted to the neurology department of the Children's Hospital Faisalabad and diagnosed with hypocalcemia. Hypocalcemia was defined as serum calcium levels < 8 mg/dL. The exclusion criteria were all the infants with seizures due to other metabolic disorders, such as hyponatremia and hypoglycemia. Infants aged less than two months or more than 2 years were excluded from the study. Infants with a prior diagnosis of epilepsy, cerebral palsy, brain tumors or malformations, head trauma, or those who had previously received calcium therapy were excluded from the study to reduce potential confounding variables. The biochemical parameters evaluated in all enrolled subjects included serum calcium, magnesium, phosphorus, parathyroid hormone, and vitamin D levels. Their normal reference ranges are given in Table 1. The status of Vitamin D was categorized as sufficient (>30 ng/mL), deficient (<20 ng/mL), and insufficient (21-29 ng/mL). Clinical information was collected by reviewing medical records, including key demographic and clinical details, such as age, sex, and comprehensive seizure characteristics (type and frequency). Data were entered and analyzed using SPSS version 24. Descriptive statistical methods were applied to summarize the findings, with frequencies and percentages calculated for categorical variables and means with standard deviations computed for continuous variables.

Table 1: Reference ranges for biochemical parameters

Parameter	Reference range
serum phosphorus	4– 7 mg/dL
serum magnesium	1.6–2.6 mg/dL
alkaline phosphatase levels	≤450IU/L
PTH levels	16–87 pg/mL

Results

A total of 54 patients with hypocalcemic fits were enrolled in the current study. Of 54 patients, males were 34 (62.96%) and females 20 (37.04%). (Figure 1) Based on age distribution, 32 (59.26%) patients were in the age group <6 months, 14 (25.93%) in the age group 6-12 months, and 8 (14.81%) in the age group >12 months-24 months. (Figure 2) Based on residency, 24 (44.44%) patients were reported from rural areas, while 30 (55.56%) patients were observed from urban areas. (Figure 3) The mean (±SD) serum calcium level was 6.07 (± 0.9) mg/dL, phosphorus 4.39 (± 1.71) mg/dL, and magnesium 1.76 (± 0.56) mg/dL. The mean (±SD) vitamin D levels were 2.49 (± 0.99) ng/mL, while the mean (±SD) PTH level was 3.11 (± 0.96) pg/mL. Less than two Seizure Episodes were observed in 25 (46.30%) patients, while more than two Seizure Episodes were observed in 29 (53.70%) patients. Based on types of fits, generalized fits were observed in 42 (77.78%) patients, while focal fits were observed in 12 (22.22%) patients. The different causes of hypocalcemic fits were observed in our study, in which hypomagnesemia was the primary cause observed in 15 (27.78%) patients, followed by vitamin D deficiency in 11 (20.37%) patients, and hypoparathyroidism in 10 (18.52%) patients, while in only one patient (1.85%) the cause of hypocalcemia was pseudo-hypoparathyroidism. (Table 2)

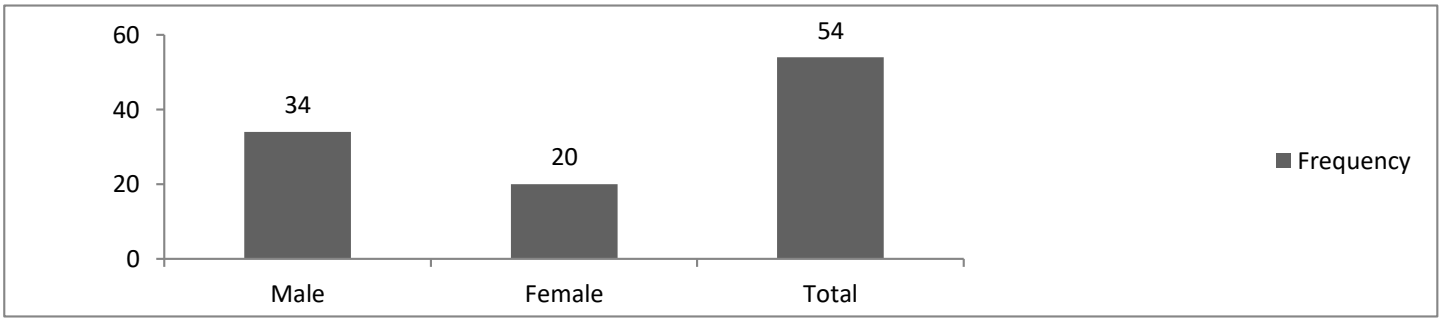

Figure 1: Patients' distribution based on gender

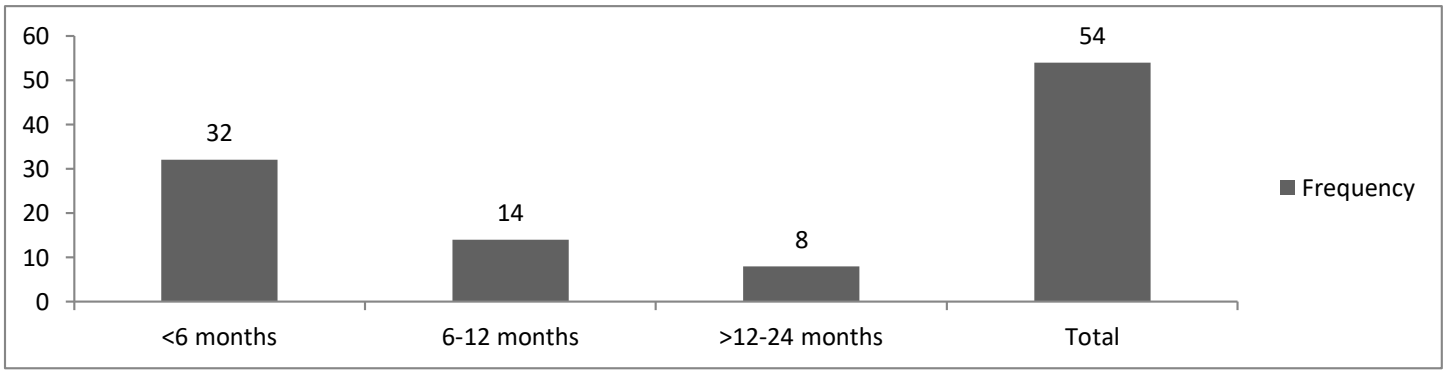

Figure 2: Patients' distribution based on age

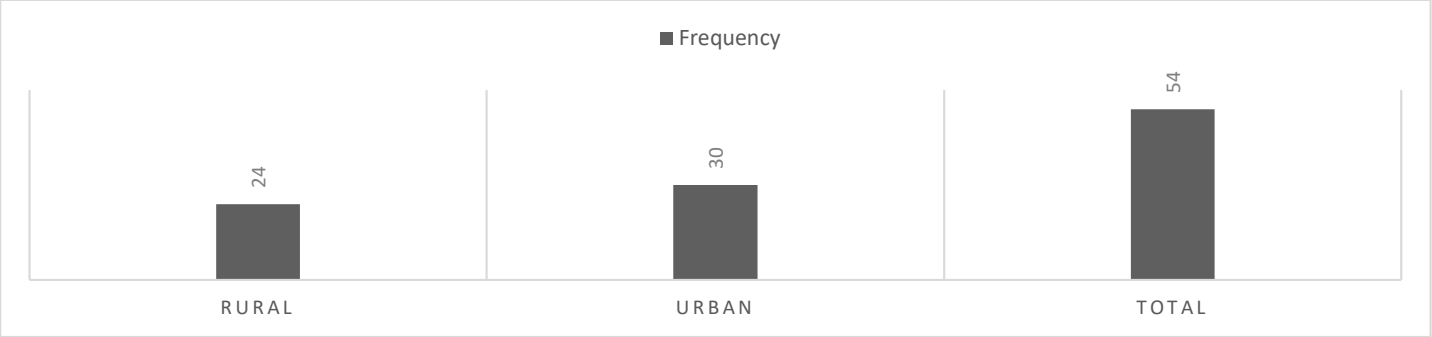

Figure 3: Patients' distribution based on residency

Table 2: Distribution of patients based on the Seizure Episodes, Types of Seizure, and Cause of Hypocalcemia

Parameter	Sub-category	Frequency
Seizure Episodes	Less than 2	25 (46.30%)
	More than 2	29 (53.70%)
Types of Seizure	Generalized	42 (77.78%)
	Focal	12 (22.22%)
Cause of Hypocalcemia	Hypomagnesemia	15 (27.78%)
	vitamin D deficiency	11 (20.37%)
	Hypoparathyroidism	10 (18.52%)
	pseudo-hypoparathyroidism.	1 (1.85%)

Discussion

Seizures are a common neurological disorder in the pediatric population (14). 4-10% of children experience at least one episode of seizures in their lives. The incidence is much higher in children under three years of age (15). Seizures are signs and symptoms resulting from high neuronal electrical activity in the brain, leading to increased muscle tone, movement, abnormal sensations, and an altered state of awareness (16). Many reasons, including metabolic disturbances, can cause afebrile seizures. Among metabolic disturbances, hypocalcemia is the most common reason (8). Calcium plays a pivotal role in neurotransmitter release at synaptic membranes and at the neuromuscular junction, as well as in muscle contraction. Hypocalcemia decreases the threshold required for neuronal activation, thus increasing neuromuscular excitability (17).

Seizures related to hypocalcemia in infants are a serious clinical concern because they carry the risk of adverse long-term neurological and developmental outcomes. The underlying causes are often multifactorial and may include hypoparathyroidism, vitamin D deficiency, hypomagnesemia, and critical systemic illnesses such as sepsis. In these conditions, disturbances in calcium and phosphorus balance are central to the pathophysiological mechanism leading to hypocalcemic seizures. The results of this study emphasize the importance of early identification and targeted treatment of underlying metabolic abnormalities to prevent significant morbidity in affected children.

A total of 54 patients with hypocalcemic fits were enrolled in the current study. Of 54 patients, males were 34 (62.96%) and females 20 (37.04%). These results are similar to those reported in earlier studies, such as those by Naz et al. and Verma et al., which also observed a higher proportion of male infants among cases of hypocalcemic seizures. The reason for this gender difference is not fully understood, but it may be related to biological factors that influence calcium homeostasis (18,19).

In our study, the mean (±SD) serum calcium level was 6.07 (± 0.9) mg/dL, phosphorus 4.39 (± 1.71) mg/dL, and magnesium 1.76 (± 0.56) mg/dL. The mean (±SD) vitamin D levels were 2.49 (± 0.99) ng/mL, while the mean (±SD) PTH level was 3.11 (± 0.96) pg/mL. These findings are consistent with a previous study by Muzna A et al., who reported similar results (20).

In our study, fewer than two seizure episodes were observed in 25 (46.30%) patients, while more than two Seizure Episodes were observed in 29 (53.70%) patients. Based on types of fits, generalized fits were observed in 42 (77.78%) patients, while focal fits were observed in 12 (22.22%) patients. These results are consistent with the findings of Kumar et al., who observed a predominance of generalized seizures among hypocalcemic infants (21). These findings are in accordance with a previous study by Muzna A et al., who reported generalized fits in the majority of their enrolled patients (20).

The different causes of hypocalcemic fits were observed in our study, in which hypomagnesemia was the primary cause observed in 15 (27.78%) patients, followed by vitamin D deficiency in 11 (20.37%) patients, and hypoparathyroidism in 10 (18.52%) patients, while in only one patient (1.85%) the cause of hypocalcemia was pseudo-hypoparathyroidism. These findings are consistent with a previous study, which reported multiple causes of hypocalcemic fits. They reported vitamin D deficiency (38.9%) as the primary cause of hypocalcemic fits in their enrolled patients, followed by hyperparathyroidism (7.4%) (20). These findings are also consistent with a previous study by Kamat et al., who reported the significant role of vitamin D in calcium homeostasis among infants (22).

The study has several notable strengths, including a thorough evaluation of biochemical markers, clearly defined inclusion criteria, and the identification of both maternal and infant risk factors. These strengths enhance the credibility of the findings and offer valuable insights for clinical practice. Nonetheless, the study has certain limitations. Its cross-sectional design restricts the ability to establish causal relationships. Incomplete documentation of maternal health parameters, particularly vitamin D status, is another limitation that could have introduced bias. Despite these constraints, the study contributes to the growing evidence on the role of vitamin D deficiency, exclusive breastfeeding without supplementation, and maternal health in the prevention of hypocalcemia-related seizures. While the findings are consistent with accessible literature, further research using larger, multicenter cohorts and prospective study designs is necessary to fill existing gaps and provide more substantial evidence for preventive and therapeutic strategies.

Conclusion

Our study concludes that hypomagnesemia, hypoparathyroidism, and vitamin D deficiency are the major causes of hypocalcemic fits. The findings highlight the importance of early detection, targeted nutritional interventions, and regular monitoring of calcium metabolism to reduce the risk of long-term complications. By identifying underlying risk factors and addressing dietary deficiencies in both mothers and infants, the study offers a basis for improving preventive strategies and enhancing clinical outcomes.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-MHGA-23)
Consent for publication
Approved
Funding
Not applicable

Conflict of interest

The authors declared no conflict of interest.

Author Contribution

AOV (Assistant Professor of Pediatric Neurology)
Manuscript drafting, Study Design,
SGN (Ex Senior Registrar)
Review of Literature, Data entry, Data analysis, and drafting articles.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the study's integrity.

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