Original Article

Prevalence of Hypocalcemia Among Infants Presenting with Seizures: A Prospective Study

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Abstract

Background: Seizures are a common neurological emergency in infancy and may result from febrile illness, epilepsy, central nervous system infection, structural brain abnormalities, or metabolic disturbances. The objective is to determine the prevalence of hypocalcemia among infants presenting with seizures. **Material and Methods:** The Department of Paediatrics at the Navodaya Medical College Hospital and Research Center in Raichur was the site of this prospective observational study. A total of 100 infants aged 1 month to 2 years presenting with seizures were included. Infants with CNS infections, known congenital brain malformations, and those whose mothers were taking drugs or supplements affecting bone mineral metabolism were excluded. **Results:** Among 100 infants presenting with seizures, 27 (27.0%) were found to have hypocalcemic seizures, while 73 (73.0%) had non-hypocalcemic seizures. Hypocalcemia due to vitamin D deficiency accounted for 27.0% of all cases and was the second most common final diagnosis after typical febrile convulsions, which were observed in 31 (31.0%) infants. Other diagnoses included atypical febrile convulsions in 20 (20.0%), epilepsy in 18 (18.0%), hypomagnesemia in 6 (6.0%), and other electrolyte abnormalities in 2 (2.0%) infants. No cases of hypoparathyroidism, hypoglycemia, CNS infection, or inborn errors of metabolism were reported. **Conclusion:** Hypocalcemia was present in more than one-fourth of infants presenting with seizures, making it an important and treatable biochemical cause in this age group. Routine corrected serum calcium estimation should be included in the initial evaluation of infants with seizures, especially in settings where vitamin D deficiency is common.

Keywords: Hypocalcemia, Infant seizures, Infants, Neonatal hypocalcemia, Serum calcium, Acute symptomatic seizures, Prospective study, Pediatric neurology.

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Introduction

Infancy is defined as the period from birth to 2 years of age.[1,2] A seizure is a transient occurrence of signs and/or symptoms resulting from abnormal excessive or synchronous neuronal activity in the brain.[3] The adjective "transient" in the definition, indicates a time frame with a clear onset and remission. Status epilepticus (SE) is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of a mechanism that leads to abnormally prolonged seizures (for a time period of 5 min or more).[4] It is a condition that can have long-term consequences (especially if its duration is more than 30 min), including neuronal death, neuronal injury, and alteration of the neuronal network, depending on the type and duration of seizures. Critical seizures that occur in children between the ages of one month and six years with a temperature increase of more than 380 degrees Celsius and no indications of an infectious condition of the central nervous system (CNS) are known as febrile seizures.[5] The most prevalent neurological issue in children with severe epilepsy that first manifests in childhood is seizures. During their first six years of life, four to ten percent of children experience at least one seizure.[6] youngsters under three years old have the highest occurrence, whereas older youngsters see a declining frequency. The causes of seizures in infancy are diverse and include febrile seizures, central nervous system infections, epilepsy syndromes, birth-related brain injury, hypoxic ischemic encephalopathy, structural brain malformations, hypoglycemia, electrolyte abnormalities, and inborn errors of metabolism.[7] Among these, metabolic disturbances are particularly important because they are often reversible and can be diagnosed through simple laboratory investigations. Electrolyte abnormalities such as hyponatremia, hypoglycemia, hypomagnesemia, and hypocalcemia may present primarily with seizures, sometimes without obvious systemic symptoms. Therefore, biochemical evaluation plays a key role in the assessment of infants presenting with seizures.[8]

Approximately 1% of all emergency department visits and 2% of

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hospital ER visits for children are caused by seizures. In children and adolescents, the incidence of epilepsy (recurrent unprovoked seizures) ranges from 50 to 100 per 100,000 person-years, and it appears to be fairly constant across all populations evaluated.[9] Childhood seizures, the most frequent fever, infections, head trauma, metabolic dysregulation, harmful prenatal events (such as stroke), and hypoxic-ischemic-encephalopathies are all caused by a variety of etiological events. Chromosome duplications and deletions, brain abnormalities caused by certain single gene mutations, and inborn metabolic mistakes are less common causes of seizures in children.[10] Synaptogenesis, dendritic arborisation, myelination, apoptosis, and priming of excess processes and synapses are all important aspects of brain development during the prenatal and early life stages.[11] Any pathologic events that occur during this early stage of life may cause intellectual disability, developmental delay, and severe brain impairment, which is frequently linked to epileptic seizures and other comorbidities. Many illnesses, including epilepsy, fever, hypoglycemia, hypoxia, hypotension, brain tumours, meningitis, electrolyte imbalance, and medication overdose, can result in seizures.[12] Seizures are one of the neurological impairments caused by severe and acute electrolyte imbalances, and they may be the only symptom that manifests. Electrolyte balance abnormalities, such as hyponatraemia, hypocalcaemia, and hypomagnesaemia, are among the multifactorial causes of seizures.[13] One of the main metabolic causes of seizures in infants is hypocalcaemia. Depolarisation is influenced by ionic calcium. The amount of depolarisation required to cause changes in sodium and potassium conductance can be lowered by a lower blood calcium concentration.[14] This makes muscle and nerve cells more excitable, which may cause seizures. Hyocalcemia can be easily detected at presentation, and if picked up early, further expensive tests like neuroimaging and invasive procedures like Lumbar puncture can be avoided.[15]

Objective: To determine the prevalence of hypocalcemia among infants presenting with seizures.

Materials and Methods

This was a prospective observational study, conducted in the Department of Pediatrics, Navodaya Medical College Hospital and Research Center, Raichur. A total of 100 infants between 1 month and 2 years of age presenting with seizures were included in the study. All infants aged 1 month to 2 years who presented with seizures to the pediatric ward of Navodaya Medical College Hospital and Research Center were enrolled after fulfilling the selection criteria. Infants aged 1 month to 2 years 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 taking drugs or supplements known to affect bone mineral metabolism were excluded.

Data Collection: After obtaining written informed consent from parents, demographic data, clinical presentation, seizure characteristics, feeding history, anthropometric parameters, and biochemical investigations were recorded in a predesigned proforma. Blood samples were collected under strict aseptic precautions and sent immediately to the central laboratory for analysis. Serum calcium, albumin, phosphorus, alkaline phosphatase, magnesium, where available, and vitamin D levels, where available, were measured. Corrected calcium was calculated using the formula: total calcium + 0.8 × (4 − serum albumin). Hypocalcemia was defined as corrected serum calcium less than 8 mg/dL.

Statistical Analysis: Data were entered in Microsoft Excel. Frequencies and percentages were used to represent categorical variables. A p-value of less than 0.05 was deemed statistically significant, and the Chi-square test and Fisher's exact test were employed for comparison. The study was prospective and carried out at Navodaya Medical College Hospital and Research Center's paediatric department., included infants aged 1 month to 2 years with seizures, and used corrected calcium <8 mg/dL to define hypocalcemia.

Results

A total of 100 infants aged 1 month to 2 years presenting with seizures were included. Among these, 27 infants (27.0%) were found to have hypocalcemia, while 73 infants (73.0%) had non-hypocalcemic seizures.

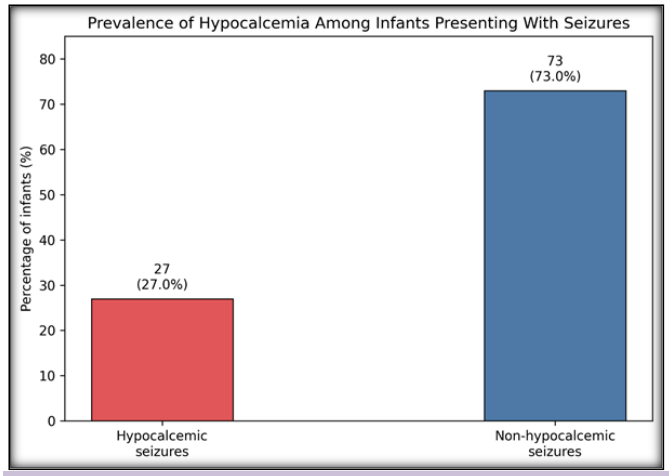

Figure 1: Prevalence of Hypocalcemia Among Infants Presenting with Seizures

Table 1: Prevalence of hypocalcemia among infants presenting with seizures

Hypocalcemic seizures	No. of infants	Percentage
Yes	27	27.0%
No	73	73.0%
Total	100	100.0%

The final diagnostic distribution showed that hypocalcemia due to vitamin D deficiency accounted for 27% of cases.

Typical febrile convulsions were the most common final diagnosis overall, observed in 31% of infants, followed by atypical febrile convulsions in 20%, epilepsy in 18%, hypomagnesemia in 6%, and other electrolyte abnormalities in 2%. No cases of hypoparathyroidism, hypoglycemia, CNS infection, or inborn errors of metabolism were reported.

Table 2: Final diagnosis among infants presenting with seizures

Final diagnosis	No. of infants	Percentage
Hypocalcemia due to vitamin D deficiency	27	27.0%
Hypomagnesemia	6	6.0%
Typical febrile convulsion	31	31.0%
Atypical febrile convulsion	20	20.0%
Epilepsy	18	18.0%
Other electrolyte abnormalities	2	2.0%
Hypoparathyroidism	0	0.0%
Hypoglycemia	0	0.0%
CNS infection	0	0.0%
Others / IEM	0	0.0%

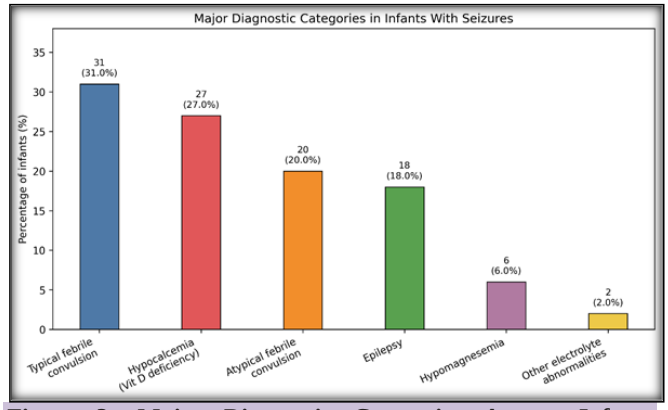

Figure 2: Major Diagnostic Categories Among Infants Presenting with Seizures

Discussion

In the present study, prevalence of hypocalcemia in infants 1 month to 2 years old presenting with seizure was assessed. Of the 100 infants studied 27 (27.0%) were identified as having hypocalcemic seizures and 73 (73.0%) non-hypocalcemic seizures. This result demonstrates that in infants that present with seizure disorder, more than a quarter of cases had hypocalcemia, which is a clinically significant biochemical cause of seizure disorder that is easily detected in this age group. The prognosis for hypocalcemia is good, so prompt diagnosis can prevent unnecessary investigations, unnecessary anticonvulsant exposure, unnecessary hospitalisation and recurrent seizures. The high number of infants with hypocalcemia in this group underscores the need for routine biochemical testing in infants who have seizures. Many conditions can cause a seizure during infancy such as febrile convulsions, epilepsy, infection of the CNS, metabolic abnormalities, electrolyte abnormalities, and structural brain lesions. Unlike many neurological disorders, however, hypocalcemia can be quickly recognized by serum calcium estimation and treated with the appropriate calcium and vitamin D therapy. This is particularly important in resource poor environments since prompt detection of hypocalcemia may avoid the need for expensive neuro-imaging or invasive investigations in individual infants with no evidence of CNS infection or structural disease.[16]

In the last diagnostic distribution 31 (31.0%) were diagnosed as typical febrile convulsions and 27 (27.0%) were diagnosed as hypocalcaemia due to a low Vitamin D level. Twenty (20.0%) infants had atypical febrile convulsions, with 18 (18.0%) being diagnosed with epilepsy. This illustrates that hypocalcemia was the second most common overall category of diagnosis and that there were more cases than epilepsy in this study population. Clinically relevant because a diagnosis of epilepsy may be made if the serum calcium is not measured at entry to the clinic.[17] All of the hypocalcemic seizure cases were attributed to hypocalcemia caused by vitamin D deficiency, implying the importance of nutrition/metabolism. Minerals, especially calcium, have a high requirement during infancy when there is a rapid rate of growth in the bones. Vitamin D deficiency affects the absorption of calcium in the gut, and may result in low serum calcium, particularly in infants who do not get enough sun, have mother who is deficient, or do not receive enough vitamin D. Breastfed infants can also be at risk if their mothers' levels of vitamin D are low since breast milk alone may not contain enough vitamin D for them to get adequate amounts, unless the mother has stored up sufficient vitamin D and is also supplemented. In addition, the lack of hypoparathyroidism, hypoglycemia, CNS infection, and inborn errors of metabolism in the final diagnosis is also noteworthy.[18] This could be due to exclusion criteria of the study, such as the exclusion of infants with CNS infection and congenital CNS malformations. It also recommends: At the onset of investigation of seizures in developmentally normal infants, common causes of reversible seizures should be strongly suspected, including hypocalcemia, hypomagnesemia and febrile convulsions. Hypomagnesemia was encountered in 6 (6.0%) cases and is also relevant since magnesium deficiency can precipitate or potentiate hypocalcemia, which is due to two effects: reduced secretion of parathyroid hormone and impaired action of PTH.[8]

This is in line with the notion that metabolic etiology of seizures is more prominent in infancy.[2,3] Calcium is important to maintain stability of the neuronal membranes and neuromuscular excitability. Low calcium decreases the threshold for depolarization and will lead to the possibility of abnormal firing of the neurons and seizures. Laboratory investigations are vital, clinically infants can have generalized seizures with no apparent indication of tetany or classical hypocalcemia. There are several limitations in this study. This was a relatively small sample size (n = 100 infants from one center), which may not be

representative of all populations. Vitamin D levels and magnesium values were only available when assessed and may not enable deeper biochemical interpretation. The study was prospective; however follow up of seizure recurrence or neurodevelopmental outcomes was not described. Further, dietary intake, maternal vitamin D levels, exposure to the sun and supplements history were not adequately considered in the results supplied, and these may have a significant effect on hypocalcemia risk.

Conclusion

This study was able to confirm that hypocalcemia is a frequent and clinically important biochemical cause of seizures in infancy. Of 100 infants with seizures between 1 month and 2 years of age, a quarter with hypocalcemic seizures were observed. Nutrient and metabolic causes of seizures were highlighted by the second most common final diagnosis after typical febrile convulsions, hypocalcemia (vitamin D deficiency). Hypocalcemia is easy to detect, treat and prevent and corrected calcium estimation should be part of the initial evaluation of infants who present with seizures. Hypocalcemia diagnosed and corrected early will assist the prevention of recurrent seizures, avoid unnecessary investigations and enhance clinical results, particularly in areas where vitamin D deficiency could be an issue.

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Conflicts of interest

There are no conflicts of interest.

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