

Original Research Article

A STUDY OF PROPORTIONS AND RISK FACTORS FOR HYPOCALCEMIA IN INFANTILE SEIZURES

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ABSTRACT

Background: Seizures are one of the most common neurological emergencies in infancy, often resulting from metabolic disturbances such as hypocalcemia. Early identification of hypocalcemia in infants presenting with afebrile seizures is crucial to guide appropriate management and avoid unnecessary investigations or interventions. This study aimed to determine the proportion and risk factors associated with hypocalcemic seizures in infants aged 1 month to 1 year.

Materials and Methods: A hospital-based prospective observational study was conducted at SMS Medical College, Jaipur, from February 2020 to December 2021. A total of 80 infants presenting with their first afebrile seizure were enrolled. Infants with known epilepsy, CNS infections, congenital brain malformations, or who had received calcium before admission were excluded. Clinical history, feeding practices, anthropometry, and laboratory parameters including serum calcium, phosphorus, alkaline phosphatase (ALP), vitamin D3, and parathyroid hormone (PTH) were evaluated. Hypocalcemia was defined as total serum calcium <8 mg/dL or ionized calcium <4.4 mg/dL. Data were analyzed using SPSS version 21, with p < 0.05 considered statistically significant.

Results: The mean age of infants was 6.5 months; 72.5% were male. Hypocalcemic seizures were observed in 27.5% of cases. Statistically significant associations with hypocalcemia included top feeding (p=0.001), inadequate sun exposure (p=0.001), and reduced night breastfeeding (p=0.001). Laboratory findings revealed higher mean phosphorus (p=0.004), ALP (p=0.042), and PTH (p=0.001), along with significantly lower vitamin D3 levels (p=0.007) in infants with hypocalcemic seizures. Calcium levels showed negative correlation with phosphorus and PTH, and a positive correlation with vitamin D3.

Conclusion: Hypocalcemia was a significant and preventable cause of afebrile seizures in 27.5% of infants. Modifiable risk factors such as feeding practices, vitamin D deficiency, and sun exposure play a critical role. Routine metabolic screening is essential in infantile seizures.

Keywords: Hypocalcemia, Afebrile seizures, Infants, Vitamin D deficiency, Risk factors, Calcium, PTH, Top feeding etc.

INTRODUCTION

Seizures are defined as transient occurrences of signs or symptoms resulting from abnormal, excessive, or synchronous neuronal activity in the brain. They can manifest as motor, sensory, behavioral, or autonomic disturbances and account for about 1–2% of all emergency department visits.^[1] Seizures are among the most common neurological disorders in the pediatric age group, affecting 4% to 10% of children at least once by 16 years of age, with the highest incidence in those under 3 years.^[2,3] The majority of childhood seizures occur during infancy (1–24 months) and tend to be brief, often presenting with focal features.^[2,3]

Globally, febrile seizures are the most common type of acute seizure in children.^[1]

Neonates are especially vulnerable, with seizures affecting about 1% of all neonates—more frequently among preterm infants—owing to immature brain function and incomplete myelination.^[4,5] The incidence ranges from 0.5–3 per 1000 live births in term infants to as high as 13% in very low birth weight preterm infants.^[4,5] According to the National Neonatal Perinatal Database (NNPD 2002–03), the overall incidence of neonatal seizures in India is 10.3 per 1000 live births, with preterm infants showing twice the risk, and very low birth weight infants showing over four times the incidence (36.1 per 1000 live births).^[6]

Acute metabolic disturbances, although accounting for only around 5% of infant seizures, are rapidly treatable and must be prioritized during initial evaluation.^[7] Among these, hypocalcemia is a leading biochemical cause of seizures in infants, especially in developing countries. Definitions of hypocalcemia vary slightly based on age and gestational maturity: in preterm infants, serum calcium <7 mg/dL and in term infants <8 mg/dL is considered hypocalcemic [8–10]. In older children, it is defined as total serum calcium below 2.1 mmol/L (8.5 mg/dL).^[11]

Hypocalcemia may present as either early or late onset. Early-onset hypocalcemia typically occurs within the first 3-4 days of life and is associated with prematurity, infants of diabetic mothers, intrauterine growth retardation, or perinatal asphyxia. Late-onset hypocalcemia, occurring after 7 days of life, is linked to causes like hypoparathyroidism, high-phosphate formula DiGeorge syndrome, mitochondrial feeding, disorders, and hypomagnesemia. While early-onset cases are often asymptomatic, symptomatic or persistent hypocalcemia should be promptly treated.^[12] Current study was undertaken to find out the proportion of hypocalcemia as a cause of seizure in infants (1 month to 1 year) admitted with first afebrile seizure.

MATERIALS AND METHODS

This hospital-based prospective observational study was conducted in the Department of Pediatrics at S.M.S. Medical College and its affiliated hospitals in Jaipur, between February 2020 and December 2021. The study aimed to determine the proportion and risk factors for hypocalcemia in infants presenting with their first afebrile seizure. The sample size was calculated assuming a 25% prevalence of hypocalcemia in such infants, with a 95% confidence level and 10% margin of error, resulting in a final sample size of 80. Infants aged between 1 month and 1 year who were admitted with a first afebrile seizure to the pediatric wards or PICU were included. Informed consent was obtained from parents or guardians. Exclusion criteria included infants with infantile spasms, those who had received prior intravenous calcium, posttraumatic seizures, known epilepsy, CNS infections, or congenital brain malformations.

A convenient sampling technique was employed until the required sample size was reached. For each enrolled infant, a detailed history and physical examination were performed, and a 2 ml blood sample was collected aseptically and sent to the central biochemistry lab within 4 hours. Serum calcium levels were measured using an automated photometric method based on the arsenazo III technique, where calcium forms a blue complex with the dye, and its intensity correlates with calcium concentration. Hypocalcemia was defined as total serum calcium <8 mg/dL (2 mmol/L) or ionized calcium <4.4 mg/dL (1.1 mmol/L). In addition to calcium, serum phosphorus, alkaline phosphatase, vitamin D, and parathyroid hormone (PTH) levels were also measured and recorded.

Operational definitions used in the study included normal serum calcium (8–10 mg/dL), vitamin D sufficiency (30–100 ng/mL), and normal PTH (10– 65 pg/mL). Ethical clearance was obtained from the Institutional Ethical Committee prior to the commencement of the study. Participants' parents were provided with study details and assured of confidentiality and voluntary participation.

Data were entered in Microsoft Excel and analyzed using SPSS version 21.0. Descriptive statistics were used for demographic and laboratory parameters. The independent t-test was used to compare means of continuous variables, chi-square test for categorical data, and Pearson's correlation for assessing associations. A p-value of <0.05 was considered statistically significant.

RESULTS

The demographic table shows the study included 80 infants with an average age of 6.5 months, predominantly male (72.5%), and mostly from Muslim (53.8%) or Hindu (42.5%) families. About one-third were malnourished, with pallor being a common clinical sign.

The birth characteristics table reveals nearly half the infants were born full-term, with most deliveries being vaginal. Over half required SNCU admission, and breastfeeding practices were concerning with only 21.3% exclusively breastfed while 76.3% received top feeding.

Laboratory parameters showed many infants had anemia (mean hemoglobin 8.8 g/dl), along with varying levels of calcium, vitamin D, and parathyroid hormone.

The outcomes data highlights that hypocalcemic seizures occurred in 27.5% of infants, with an overall mortality rate of 31.3%.

Religion was the only demographic factor significantly associated with seizures, with Hindu

infants showing higher seizure rates compared to Muslim infants.

Several feeding practices significantly correlated with hypocalcemic seizures: top feeding, lack of night breastfeeding, and inadequate sun exposure all increased seizure risk.

Laboratory comparisons revealed infants with hypocalcemic seizures had significantly higher

phosphorus, alkaline phosphatase, and PTH levels, but lower vitamin D levels compared to those without seizures.

Correlation analysis demonstrated that calcium levels were inversely related to phosphorus and PTH levels and directly related to vitamin D levels, suggesting important metabolic relationships in calcium regulation.

Table 1: Demographic and Clinical Characteristics of Participants (n=80)		
Characteristic	Value	
Age	Mean: 6.5 months (SD 2.8)	
Gender	Male: 58 (72.5%), Female: 22 (27.5%)	
Religion	Muslim: 43 (53.8%), Hindu: 34 (42.5%), Christian: 3 (3.8%)	
Nutritional Status	Normal: 53 (66.3%), Malnourished: 27 (33.8%)	
Clinical Signs	Pallor: 30 (37.5%), Edema: 14 (17.5%), Cyanosis: 2 (2.5%)	

Table 2: Birth and Feeding Characteristics of Participants

Characteristic	Value
Gestation	Full term: 39 (48.8%), Preterm: 26 (32.5%), Late preterm: 15 (18.8%)
Mode of delivery	Normal vaginal: 49 (61.3%), LSCS: 31 (38.8%)
Birth weight	Mean: 2.46 kg (SD 0.34)
SNCU admission	42 (52.5%), Mean duration: 6.24 days (SD 3.62)
Breastfeeding practices	Exclusive: 17 (21.3%), Partial: 63 (78.8%), Within first hour: 24 (30%)
Top feeding	61 (76.3%), Dilution practiced: 41 (51.2%)

Table 3: Table 3: Laboratory Parameters of Participants

Parameter	Mean	SD	Range
Hemoglobin (g/dl)	8.8	2.3	4.2-12.8
Calcium (mg/dl)	9.0	1.2	5.1-11.4
Phosphorus (mg/dl)	7.4	1.9	2.4-12.2
ALP (mg/dl)	519.8	203.4	125.0-1190.0
Vitamin D3 (ng/dl)	25.9	11.5	11.8-108.5
PTH (pg/ml)	152.21	116.43	2.5-687.0

Table 4: Table 4: Incidence of Hypocalcemic Seizures and Outcomes			
Parameter	Frequency	Percent	
Hypocalcemic seizures	22	27.5%	
Final outcome			
Discharged	55	68.8%	
Expired	25	31.3%	

Table 5: Association of Hypocalcemic Seizures with Demographic Factors			
Factor	Seizures Present (n=22)	Seizures Absent (n=58)	p-value
Age			
1-6 months	13 (59.1%)	24 (41.4%)	0.156
>6 months	9 (40.9%)	34 (58.6%)	
Gender			
Female	10 (45.5%)	30 (51.7%)	0.617
Male	12 (54.5%)	28 (48.3%)	
Religion			
Hindu	13 (59.1%)	21 (36.2%)	0.030*
Muslim	7 (31.8%)	36 (62.1%)	
Christian	2 (9.1%)	1 (1.7%)	

Table 6: Association of Hypocalcemic Seizures with Feeding Practices and Sun Exposure

Factor	Seizures Present (n=22)	Seizures Absent (n=58)	p-value
Top feeding	16 (72.7%)	25 (43.1%)	0.001*
Night breastfeeding	11 (40.9%)	38 (65.5%)	0.001*
Adequate sun exposure	9 (40.9%)	33 (56.9%)	0.001*
Exclusive breastfeeding	6 (27.3%)	21 (36.2%)	0.158
Breastfeeding after 1 hour of delivery	8 (36.4%)	16 (27.6%)	0.444

Table 7: Comparison of Laboratory Parameters Between Infants with and Without Hypocalcemic Seizures			
Parameter	Seizures Present (n=22)	Seizures Absent (n=58)	p-value
Phosphorus (mg/dl)	8.3 ± 2.3	7.0 ± 1.5	0.004*
ALP (mg/dl)	544.0 ± 134.5	510.6 ± 224.4	0.042*
Vitamin D3 (ng/dl)	20.3 ± 4.9	28.0 ± 12.6	0.007*
PTH (pg/ml)	222.7 ± 189.1	125.4 ± 54.3	0.001*

Table 8: Correlation of Serum Calcium with Other Parameters			
Parameter	Correlation Coefficient	p-value	
Phosphorus	-0.355	0.001*	
Vitamin D3	0.276	0.013*	
PTH	-0.330	0.003*	
ALP	-0.122	0.282	

DISCUSSION

The present study examined hypocalcemia as a cause of seizures in infants aged 1 month to 1 year admitted with first afebrile seizure. Our hospital-based prospective observational study included 80 infants admitted to pediatric wards and intensive care units after obtaining written consent from parents/guardians.

Seizures represent a common pediatric neurological disorder, with 4-10% of children experiencing at least one episode in their first 16 years.^[13] Unlike adult seizures, infant seizures are rarely idiopathic, with identifiable causes in 99% of cases. Hypocalcemia represents an important treatable cause, and early diagnosis can avoid expensive neuroimaging, invasive procedures like lumbar puncture, and unnecessary antiepileptic medications. Our study population had a mean age of 6.5 months (SD 2.8), with 43 infants above 6 months. This is comparable to other studies: Rehman et al.^[14] reported a mean age of 10.58 months, Kamate et al,^[15] reported 9.5 months,. Males predominated (72.5%), consistent with other studies showing male predominance: Rehman et al,^[14] (52.98%), Kamate et al,^[15] (65.4%), and Gowda et al,^[16] (58%). This reflects the general male-female ratio in our country. Anthropometrically, our participants had a mean weight of 5.8 kg (SD 1.4) and mean height of 61.0 cm (SD 7.9). Mean birth weight was 2.5 kg (SD 0.34). Regarding maternal education, 50% had only primary education, consistent with Rehman et al,^[14] who reported 51.8% illiterate mothers.

The religious distribution showed 53.8% Muslim and 42.5% Hindu participants, with 52.5% from nuclear families. Most families (37.5%) had 2 children, followed by 32.5% with 3 children.

Regarding gestational age, 48.9% were full-term, 18.8% late pre-term, and 32.5% pre-term. This differs from Manzoor Ali et al,^[17] who reported only 17.1% preterm infants, possibly due to our larger sample size. Most infants (61.3%) were delivered vaginally, with 91.3% born in hospitals, reflecting increased awareness about institutional deliveries.

In our study, hypocalcemic seizures occurred in 27.5% of infants, showing no significant association with age (p>0.156) or gender (p=0.617). However, significant associations were found with top feeding (p=0.001), inadequate sun exposure (p=0.001), and lack of night breastfeeding (p=0.001). Laboratory parameters revealed significantly higher phosphorus (p=0.001), alkaline phosphatase (p=0.004), and parathyroid hormone (p=0.001) levels, but lower vitamin D3 (p=0.007) in hypocalcemic infants. Calcium showed significant negative correlations

with phosphorus (p=0.001) and PTH (p=0.003), and positive correlation with vitamin D3 (p=0.013).

These findings align with previous research. Rehman et al,^[14] found hypocalcemic seizures in 24.7% of children with first afebrile seizures, predominantly in the 2-12 month age group (68%, p=0.084), males (53%, p=0.146), and those with inadequate sunlight exposure and illiterate mothers (p=0.01). Khan et al,^[17] reported even higher rates (68%) and identified unfortified fresh milk consumption, inadequate sun exposure, lower maternal education, and large family size as risk factors.

Other studies reported varying but significant proportions: Kamate et al,^[15] found hypocalcemia accounting for 25% of seizures in children aged 1 month to 2 years (p=0.001); Nikunj et al,^[18] reported 34% (p=0.001); and Gowda et al,^[16] reported 12% (p=0.0018).

The association with vitamin D deficiency is particularly notable. Mehrotra et al,^[51] observed strong positive correlations between maternal and infant vitamin D levels (p<0.001), with 89% of infants with severe deficiency born to similarly deficient mothers. Salama et al,^[19] found 72% of infants had vitamin D levels below 20 ng/mL, with mothers of hypocalcemic seizure infants having severe vitamin D deficiency (p=0.005).

Poor outcomes are associated with hypocalcemia, as measured by survival or length of intensive care stay. Infants fed buffalo or cow's milk or high-phosphate formula show decreased calcium absorption due to phosphate interference. Balasubramanian et al,^[20] identified indoor confinement, urban living with tall buildings, and sunscreen use as major risk factors, while others have highlighted unfortified milk, inadequate sunlight exposure, low maternal education, and large family size as contributing factors.

CONCLUSION

Current study concluded that proportion of hypocalcemic seizure was 27.5% and association of hypocalcemic seizure. Hypocacemic seizure were associated with demographic risk factors like top feeding, inadequate sun exposure, male gender, low maternal education with low night breastfeeding. Laboratory parameters like high phosphorous, high alkaline phosphatase and high PTH with low value of Vit D3 were associated with hypocalcemia.

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