Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/bdndmq73

AN OBSERVATIONAL RESEARCH FOR HYPOCALCEMIC FITS IN KIDS WHO ARRIVE AT A TERTIARY CARE HOSPITAL WITH AFEBRILE CONVULSIONS.

Mubashir Raza[1*], Muhammad Azhar[2], Arshad Ali Lakho[3], Ishrat Fatima[4], Abdul Raziq[5], Zulfiqar Ali Dahri[6]

[1*,2,4]Consultant Paediatrician, RHQ Hospital Skardu, Pakistan.
[3]Assistant Professor Pediatric Medicine, People's University of Medical & Health Science, Nawabshah, Pakistan.
[5]Consultant Paediatrician, District Children Specialist Women & Children Hospital Kohat. Pakistan.
[6]Consultant Paediatrician, Institute of Mother & Child Health Nawabshah, Pakistan.

***Correspondence Author:** Mubashir Raza
*Consultant Paediatrician, RHQ Hospital Skardu, Pakistan. Email: Mubashirraza88@gmail.com

ABSTRACT

Introduction: A seizure without fever is known as an afebrile seizure. Hypocalcemia is the most frequent metabolic anomaly producing afebrile seizures in children. Children with hypocalcemia may not exhibit any symptoms at all or they may exhibit a variety of signs and symptoms. Very young patients are more prone to exhibit symptoms including weakness, feeding issues, facial spasms, jitteriness, or seizures because they are unable to appropriately describe their symptoms verbally.
Aims & Objectives: To ascertain how frequently afebrile seizures in children are associated with hypocalcemic fits.
Materials & Methods: A descriptive cross-sectional study in which a total of 106 children presented during a span of 06 months i.e. May 2019 to November 2019 with the afebrile seizure of age 1-60 months in the pediatric department of the Children Hospital Pims Islamabad were included. The patient's blood sample was drawn at the time of presentation and sent to the hospital laboratory for biochemical analysis of serum calcium.
Results & Findings: Age ranged from 1 to 60 months in this study, with a mean age of 23.28 12.56 months. The bulk of the 80 patients (75.47%) were infants under the age of one year. 40 of the 106 patients were female and 66 (62.26%) were male, making a male to female ratio of 1.65:1. According to this study, there are 15 (14.15%) hypocalcemic fits per 1,000 children who arrive with afebrile convulsions.
Conclusion: This study came to the conclusion that children who appear with afebrile seizures frequently experience hypocalcemic fits.

Keywords: afebrile seizures, serum calcium, hypocalcemia.

INTRODUCTION:

Seizures can be defined as a sudden change in behavior, characterized by an alteration in sensory perception or motor activity that results from excessive and synchronous electrical firing in groups of neurons. [i] The incidence is highest in children younger than 3 years of age, with a decreasing frequency in older children. Seizures are the most common disorder of the central nervous system in

childhood with 4-10% of children experiencing at least one seizure within first 16 years of life constituting significant number of admissions to the pediatric emergency departments.[ii,iii] A laboratory and clinical condition known as hypocalcemia is seen very frequently, particularly in newborn and paediatric patients. Laboratory hypocalcemia is frequently asymptomatic, and treating it in newborns is debatable. But in paediatric intensive care units , children with hypocalcemia had greater mortality rates than kids with normal calcium levels.[iv] A total blood calcium level in children is considered hypocalcemic if it is less than 2.1 mmol/L (8.5 mg/dL).Hypocalcemia is defined as either an ionised fraction of less than 1.1 mmol/L (4.4 mg/dL) or a total serum calcium concentration of less than 2 mmol/L (8 mg/dL) in term newborns.Infants weighing less than 1500 g at birth are considered to have hypocalcemia if their total blood calcium content is less than 1.75 mmol/L (7 mg/dL). When the ionised calcium level drops below 0.8-0.9 mmol/L, symptoms frequently appear.[v] Depending on the child's age at presentation, different hypocalcemia causes can be identified. Prematurity, birth asphyxia, intrauterine growth restriction, and babies of diabetic mothers are the causes of early neonatal hypocalcemia, which manifests within 48–72 hours of birth.The causes of late-onset neonatal hypocalcemia which typically occurs 3-7 days after birth are exogenous phosphate load, vitamin D deficiency, primary immunodeficiency disorder like Digeorge syndrome, magnesium deficiency, transient hypoparathyroidism of the newborn, hypoparathyroidism due to other causes maternal hyperparathyroidism, blood transfusion or sodium bicarbonate infusion, and phototherapy for hyperbilirubinemia. [vi]Among the factors contributing to hypocalcemia in young children and newborns include hyperphosphatemia, hypoparathyroidism, and aberrant vitamin D synthesis or action.[vii] In a study by Naz et al, it is showed that frequency of hypocalcemia was 62.5% in children presenting with afebrile seizures.[viii] Only two studies were found by us in our country and we conducted this study on 106 patients.

METHODOLOGY:

This cross-sectional study was carried out at The Children Hospital in Islamabad's pediatrics department from May 9 to November 8, 2019.Sample size was calculated with WHO calculator that is 106 with confidence level of 95%,Absolute precision 6%, Anticipated population proportion 11.1%[ix]. The Inclusion criteria was children who presented with afebrile seizure (abnormal body movements in a children occurring in absence of fever body temperature ≤ 99.6°F) it was diagnosed clinically on history at the time of presentation), age 1 – 60 months and both genders with exclusion criteria of known cases of epilepsy, children who have already received intravenous calcium, children with seizures onset after hospitalization, parents/guardian who are not willing to participate in the study.

The study was conducted after approval and permission from Hospital Ethical Committee. Patients presenting with afebrile seizures and fulfilling the inclusion/exclusion criteria of our study were included in the study after taking an informed written consent from the parents or guardians of child. Clinical history and detailed demographic details were taken by the trainee researcher. Complete physical examination of the patient was performed. Blood sample of the patient was drawn at the time of presentation to the hospital and was sent to the hospital laboratory for biochemical analysis of serum calcium. All the data collection was performed by the trainee researcher himself to maintain data quality and compliance. All the study results were recorded on a proforma. Data was entered and analyzed by computer software SPSS Version

20.0. Frequencies and percentages were calculated for qualitative variables, such as gender, feeding pattern, exposure to sun light, Socioeconomic (SE) status and frequency of hypocalcaemia. Mean ± standard deviation was calculated for quantitative variables such as age and serum calcium level. Effect modifiers like age, gender, exposure to sun light and SE status were controlled by the stratification. Post stratification chi-square test was applied and P-value < 0.05 was considered significant.

RESULTS & FINDINGS

Age in this study was from 1-60 months with mean age of 23.28 ± 12.56 months. Majority of the patients 80 (75.47%) were between 1-30 months of age as shown in Table I. Out of 106 patients, 66 (62.26%) were males and 40 (37.74%) were females with male to female ratio of 1.65:1. Mean serum calcium levels were
9.68±2.39 mg/dl. Distribution of patients according to sun exposure and socioeconomic status is shown in Table II & III respectively. This study has shown the frequency of hypocalcemic fits in children presenting with afebrile seizures as 15 (14.15%). Stratification of hypocalcemia with respect to age groups and gender is shown in Table IV & V respectively. Stratification of hypocalcemia with respect to sun exposure and socioeconomic status is shown in Table VI & VII respectively.

Table-I: Distribution of patients according to Age (n=106). Age (in months)

	No. of Patients	*%age*
1-30 months	80	75.47
31-60 months	26	24.53
Total	**106**	**100.0**

Mean ± SD = 23.28 ± 12.56 months

Table-II: Distribution of patients according to sun exposure (n=106).

Sun exposure	***No. of atients***	***%age***
≤2 hours	45	42.45
>2 hours	61	57.55
Total	**106**	**100.0**

Table-III: Distribution of patients according to socioeconomic status (n=106).

SES	***No. of Patients***	***%age***
Poor	39	36.79
Middle	54	50.94
High	13	12.27

Table IV: Stratification of Hypocalcaemia with respect to age groups.

Age groups	***Hypocalcaemia***	
	Present	**Absent**
1-30 months	10	70
31-60 months	05	21
P-value	**0.392**	

Table V: Stratification of Hypocalcaemia with respect to gender.

Gender	***Hypocalcaemia***	
	Present	**Absent**
Male	11	55
Female	04	36
P-value	**0.340**	

Table VI: Stratification of Hypocalcaemia with respect to sun exposure.

Sun Exposure	*Hypocalcaemia*	
	Present	**Absent**
≤2 hours	06	39
>2 hours	09	52
P-value	**0.836**	

Table VII: Stratification of Hypocalcaemia with respect to socioeconomic status.

socioeconomic status	*Hypocalcaemia*	
	Present	**Absent**
Poor	06	33
Middle	09	45
High	00	13
P-value	**0.290**	

DISCUSSION:

A seizure or convulsion is a brief, paroxysmal change in the way a person moves or behaves as a result of aberrant brain electrical activity. Around 10% of children in the paediatric age range experience seizures, which are common..[x] Seizures may not necessarily indicate the presence of a problem of the central nervous system caused by systemic or metabolic changes, but they are a symptom of such a disorder.[xi] Hypocalcemia is the most frequent metabolic imbalance that results in seizures in children, and it can cause tetany, seizures, cramps in the muscles, and paresthesia.[xii]

This study has shown the frequency of hypocalcemic fits in children presenting with afebrile seizures as 15 (14.15%). Taherian R et al in their study determined the main etiologies of seizure in children and their results showed that 11.11% (4/36) of the patients with afebrile seizures had hypocalcaemia.

Hyponatremia and Hypoglycemia was present in 11.11% (4/36) and 33.33% (12/36) of the patients respectively. They further ruled out that all the children diagnosed with hypocalcaemic fits were under the age of 3 years.[ix] A local study found that out of 86 instances, 55% (n=47) were between the ages of 2 and 12 months and 45% (n=39) were between the ages of 13 and 24 months (mean was 66 12.33+5.27 months). Maternal age data reveals that 52.38% of mothers (n=44) were male and 47.62% of mothers (n=42) were female, with 72.24% of mothers (n=58) between the ages of 18 and 30 and 30.76% of mothers (n=29) between the ages of 31 and 45. 66.48% (n=56) of children with afebrile seizures between the ages of 2 months and 2 years had hypocalcaemia frequently..[xiii]Study done by alber et al reported that 65% children having fever free fits which support our results[xiv]. Binmahana et al also report 72.2% a febrile hypocalcaemia fits.[xv] Many patients at metropolitan referral hospitals in underdeveloped nations suffer from febrile fits brought on by hypocalcaemia.[xvi,xvii] The clinical, biochemical, and radiological results of 13 patients with hypoparathyroidism (mean age: 9 years) were described by Mithal et al. in 1989. In 1989, Mithal et al. reviewed the clinical, biochemical, and radiological outcomes of 13 hypoparathyroid patients (mean age: 9 years). At the time of admission, two patients were experiencing an acute hypocalcemic crisis, and nine patients had a history of generalized seizures. Five of the nine individuals who had head computed tomography scans had basal ganglia calcification that could be seen.[xviii] In a research study carried out at neonatal ward, Dhaka Bangladesh in 2003 and 2004, 60% of cases had hypocalcemia while only 20% of the controls had hypocalcemia.[xix] The Odd ratio was 6 times more in cases in Bangladeshi study. Another international study showed that out of 51 cases only 8

(15.7%) had hypocalcemia as cause of neonatal fits.[xx] When all etiological factors were taken into account for the seizure's cause in a study by Faridullah et al. at the neonatal unit of the Hayatabad Medical Complex in Peshawar, hypocalcemia was shown to be responsible for just 12.5% of the seizures.[xxi] Because hypocalcemia is linked to poor outcomes, as assessed by either survival or length of critical care stay, maintaining normal calcium levels is crucial.[xxii]The majority of our vitamin D requirements are met by incidental sun exposure during daily activities; as a result, sunshine is crucial for preserving calcium homeostasis.[xxiii] Infants who are fed buffalo or cow milk or formula with high phosphate content frequently develop hypocalcemia. The risk factors for hypocalcemia have been identified by both international and local investigations. Low maternal vitamin D levels, daytime confinement indoors, residing in metropolitan regions with tall buildings, and sunscreen use were all noted as substantial risk factors by Balasubramanian et al. in India. Fresh unfortified milk, poor sun exposure, low maternal education, and high family size were identified as risk factors for hypocalcemia by Humayun et al. in Pakistan.[xxiv] In a study of 60 newborns with hypocalcemic seizures (15 days to 6 months of age), Mehrotra et al. discovered low levels of Vitamin D (10 ng/ml) in 54 of the infants, drawing the conclusion that Vitamin D insufficiency is a primary cause of infantile hypocalcemic seizures and a risk factor for hypocalcemia..[xxv] Another study found that 35.15 percent (n=19) of seizures had hypocalcemia as a contributing factor, and in 78.9 percent (n=15) of these infants, inquiry results point to Vitamin D deficiency.[xxvi]

The majority of research on a child's first non-febrile seizure has produced very few aberrant lab test results. The outcomes of laboratory investigations did not aid in the diagnosis or treatment in two studies of febrile and non-febrile seizures [xxvii]However, in another study, 68 mainly in infants younger than six months, 10% of the 65 children with new-onset afebrile convulsions had either hyponatremia or hypocalcemia.[xxviii] Previous research from underdeveloped nations also indicates that hypocalcemia is frequently to blame for baby seizures. [xxix] When examining the first seizures in non-epileptic children, electrolyte abnormalities such hypocalcemia should be taken into account, especially in individuals with protracted irritability and elevated muscle tone. Vitamin D insufficiency, hypomagnesemia, hypophosphatemic rickets, vitamin D- dependent rickets, malabsorption, and renal and hepatic failure are among the possible differential diagnoses for hypocalcemia. When low calcium levels are coupled by elevated alkaline phosphatase, elevated PTH, and decreased vitamin D levels, nutritional vitamin D deficiency is diagnosed. Due to the extremely low serum calcium levels, elevated PTH, and lowered vitamin D levels, nutritional rickets was confirmed.[xxx] Few aberrant laboratory test results have been found in the majority of investigations on children's first non-febrile seizures. Results of laboratory investigations did not aid in the diagnosis or treatment in two studies of febrile and non-febrile seizures.[xxxi,xxxii] However, in a different study of 65 toddlers with newly developing afebrile seizures, 10% of the children, predominantly those under the age of six months, exhibited either hyponatremia or hypocal cemia.[xxxiii]

Hypocalcemia can present with a wide variety of symptoms, the most important of which are seizures. In 90% of cases, seizure type was noted generalized tonic colonic which was comparable with Sharma et.[xxxiv]53.3% of patients had elevated alkaline phosphatase > 1000 1U/L, which is consistent with earlier research. Intravenous calcium should be used to treat hypocalcemic seizures. Because calcium gluconate is less irritant and less likely to result in tissue necrosis if extravasation occurs, it is favoured over calcium chloride. High dose vitamin D (150,000–300,000 units) should be administered intramuscularly to treat vitamin D deficiency before being followed by calcium and vitamin D taken orally.[xxxv]

Conclusion

This study came to the conclusion that children who appear with afebrile seizures frequently experience hypocalcemic fits. In order to lower the morbidity of children, we advise that this

condition be identified and managed early on. In order to handle children with hypocalcemia early and prevent complications, clinicians can also organise public awareness campaigns on a national and regional level.

References

1. Teran F, Harper-Kirksey K, Jagoda A. Clinical Decision Making In Seizures And Status Epilepticus. Emerg Med Pract. 2015;17:2-7
2. Berg AT, Jallon P, Preux PM. The epidemiology of seizure disorders in infancy and childhood: definitions and classifications. Handb Clin Neurol. 2013;111:391-8.
3. Mwipopo EE, Akhatar S, Fan P, Zhao D. Profile and clinical characterization of seizures in hospitalized children. Pan Afr Med J. 2016;24:313-6.
4. Steele T, Kolamunnage-Dona R, Downey C, Toh CH, Welters I.Assessment and clinical course of hypocalcemia in critical illness. Crit Care. 2013;17(3):R106.
5. Vuralli D. Clinical Approach to Hypocalcemia in Newborn Period and Infancy: Who Should Be Treated?. Int J Pediatr. 2019;2019:4318075.
6. Tsang RC, Chen I, Hayes W, Atkinson W, Atherton H, Edwards N. Neonatal hypocalcemia in infants with birth asphyxia. J Pediatr. 1974 Mar. 84(3):428-33.
7. Venkataraman PS, Tsang RC, Chen IW, Sperling MA. Pathogenesis of early neonatal hypocalcemia: studies of serum calcitonin, gastrin, and plasma glucagon. J Pediatr. 1987 Apr. 110(4):599-603.
8. Naz I, Naeem HMM, Ikram S, Naz M, Usman M, Rehman A. Hypocalcemia in Children Presenting with Afebrile Seizures. Pakistan J. Medical Health Sci.. 2022 Jul 30;16(7):711–2
9. Taherian R, Feshangchi-Bonab M, Rezayi A, Jahandideh M. The Etiologic Profile of the Pediatric Seizure: An Epidemiological Study from Iran. Int Clin Neurosci J. 2017;4:98-102.
10. Johnston MV. Seizures in childhood. In Behrman RE, Kliegman RM, Jenson HB. Nelson textbook of Paediatric. 18 th ed. Philadelphia : WB Saunders 2008: 2457- 75.
11. Sood A, Grover N, Sharma R. Biochemical abnormalities in neonatal seizures. J Pediatr 2003; 70: 221-4
12. Singh SC, Singh J, Prasad R. Hypocalcemia in Paediatric care unit. J Pediatr 2003; 49: 298-302
13. Rehman M, Bajwa FE, Mushtaq MA, Sarwar I, Amir S, Nawaz R. Afebrile seizures; frequency of hypocalcemia in children presenting with afebrile seizures. Professional Med J 2019; 26(5):836-840.
14. Dibbens LM, Reid CA, Hodgson B. Augmented currents of an HCN2 variant in patients with febrile seizure syndromes. Ann Neurol 2010; 67(4):542-6.
15. Egri C, VilinYY, Ruben PC. Thermoprotective role of the sodium channel ß1 subunit is lost with the ß1 (C121W) mutation. Epilepsia 2012; 53(3):494-505.
16. Radzicki D, YauHJ, Pollema-Mays SL. Temperaturesensitive Cav1.2 calcium channels support intrinsic firing of pyramidal neurons and provide a target for the treatment of febrile seizures. J Neurosci 2013; 33(24):9920-31.
17. Salam SM, Rahman HM, Karam RA. GABRG2 gene polymorphisms in Egyptian children with simple febrile seizures. Indian J Pediatr 2012; 79(11):1514-6
18. Mithal A, Menon PS, Ammini AC, Karmarkar MG, Ahuja MM. Spontaneous hypoparathyroidism: Clinical, biochemical and radiological features. Indian J Pediatr. 1989;56:267–72.
19. Baten OS, Mollah AH, Ali MN ,Rashid MH. Serum Calcium Status of Neonates with Seizure in a Tertiary Care Hospital . Bangladesh J Child Health 2012;36(3):122-12.
20. Pravin R, Salim A, Rahman M, Chowdhry K, Sultana K, Ahmed S, Rahman Z. Neonatal seizures: Correlation between Clinic-Etiological profile and EEG findings. Bangladesh J Child Health 2014;38(1):19-23.
21. Shah FU, Jahanzeb M ,Khan MA. Etiological study of Neonatal seizures in neonates. Khyber Med Uni J 2013;5(1):9-12.

22. Khan HI, Abdullah A, Kazi MY, Afzal MF. Hypocalcemia and nutritional rickets in children: common etiological factors. Ann King Edward Med Coll 2006; 12 (1): 29-32
23. Hatun S, Ozkan B, Orbak Z, Doneray H, Cizmecioglu F, Toprak et al. Vitamin D deficiency in early infancy. J Nutr 2005; 135: 279-82
24. Johnston MV. Seizures in childhood. In Behrman RE, Kliegman RM, Jenson HB. Nelson textbook of Paediatric. 18 th ed. Philadelphia : WB Saunders 2008: 2457- 75.
25. Mehrotra P, Marwaha RK, Aneja S, Seth A, Singla BM, Ashraf G, et al. Hypovitaminosis d and hypocalcemic seizures in infancy. Indian Pediattic 2010;47:581-6
26. Bande B, Agrawal A. Study of incidence of hypocalcemia in infants admitted with seizures in a tertiary care hospital. Indian J Child Health. 2018; 5(11):674-677
27. Smith RA, Martland T, Lowry MF. Children with seizures presenting to accident and emergency. J Accid Emerg Med. 1996; 13:54-8.
28. Huang CC, Chang YC, Wang ST. Acute symptomatic seizure disorders in young children – a population study in southern Taiwan. Epilepsia. 1998;39:960-4
29. Nypaver MM, Reynolds SL, Tanz RR, Davis T. Emergency department laboratory evaluation of children with seizures: dogma or dilemma? Pediatr Emerg Care. 1992; 8: 13-16.
30. Cooper MS, Gittoes NJ. Diagnosis and management of hypocalcaemia. BMJ 2008; 7; 336: 1298-302.
31. Smith RA, Martland T, Lowry MF. Children with seizures presenting to accident and emergency. J Accid Emerg Med. 1996; 13:54-8.
32. Nypaver MM, Reynolds SL, Tanz RR, Davis T. Emergency department laboratory evaluation of children with seizures: dogma or dilemma? Pediatr Emerg Care. 1992; 8: 13-16
33. Garvey MA, Gaillard WD, Rusin JA, Ochsenschlager D, Weinstein S, Conry JA, et al. Emergency brain computed tomography in children with seizures: who is most likely to benefit? J Pediatr. 1998; 133:664-9
34. Sharma J, Bajpai A, Kabra M, Menon PS. Hypocal-cemia – clinical biochemical radiological profile and follow up in a tertiary hospital in India. Indian Pediatr 2002; 39: 276- 82.
35. elHaq AI, Kanzar ZA. Neutritional vitamin D deficiency rickets in Saudanes children. Ann Trop Paediatr 1995; 15: 69-76