

Original Research Article

Frequency of Hypocalcaemia among Children (age 2-60 months) presenting with first episode of afebrile seizures: A cross sectional study

Abstract

Aim: To determine the frequency of hypocalcaemia among children aged 2 to 60 months presenting with afebrile seizures.

Study Design: A cross sectional study.

Place and duration: Department of Pediatrics, Liaquat University of medical and Health Sciences Jamshoro, from February to August-2020

Methodology: A total of 130 children aged 2 to 60 months, having afebrile fits with birth weight more than 2.5 kg were enrolled. After taking full history, detailed examination was done. Two ml blood sample was taken from each patient and was sent to diagnostic laboratory of the institution to find out calcium levels. In case of proven hypocalcaemia, injection calcium gluconate 100mg/kg was administered. Mean and standard deviation were calculated for quantitative variables while frequency and percentages were noted for qualitative variables. Frequency of hypocalcaemia was recorded and study variables were compared between children with and without hypocalcaemia.

Results: Majority of the patients, 69 (53.1%) were male, 64 (49.2%) less than or equal to 12 months of age, 28 (21.5%) had maternal educational status as illiterate, 78 (60.0%) belonged to rural areas, 59 (45.4%) belonged to middle socioeconomic status, 69 (53.1%) had poor exposure

to sunlight, 80 (61.5%) had malnutrition, 82 (63.1%) had child spacing of less than 2 years, 79 (60.8%) with less than 5 episodes of fits per day and 88 (67.7%) had duration of fits per day as less than 5 minutes. Frequency of hypocalcaemia was noted in 81 (62.3%) cases.

Conclusion: We concluded that hypocalcaemia is the frequent cause of afebrile seizures in children aged 2 to 60 months.

Keywords: Hypocalcaemia, afebrile fits, malnutrition, poor exposure to sunlight.

Introduction:

We are familiar with the febrile seizure but the terminology of afebrile seizures are becoming common in pediatrics. It refers to provoked seizures in children, who don't have any element of fever. ¹ Many kinds of seizures occur in children, in addition, these children may develop additional afebrile seizure. ² When seizures occur without fever, medical evaluation is needed to identify the causes. Seizures are labelled as unprovoked, when there is no precipitating factor. ³ Incidence of unprovoked seizures is 41-63 cases per 100,000 per year. ⁴ About 30% of unprovoked seizure occurs due to brain injury or due to progressive neurologic disorder. ⁵

As there are many causes of afebrile seizures, that's why proper history, detailed neurological examination along with electroencephalography and neuroimaging is required to reach the diagnosis. There is no need to start anti-convulsions drugs after the first episode of afebrile seizures. ⁶ Viral gastroenteritis is a well-known cause of afebrile seizures and it is becoming a separate entity. ⁷ One of the cause of afebrile seizure is hypocalcemia. ⁸ Although hypocalcemia may be due to hypoparathyroidism, but it is rare. It results in hypocalcemia, hyperphosphatemia and calciuria. ⁹

Vitamin D and parathyroid hormone plays an important role in the calcium hemostasis.

Hypocalcemia increases the production of 1, 25- dihydroxyvitamin D, hence it is controlled by the serum calcium level.¹⁰ Serum calcium level directly controls the enzyme responsible for synthesizing 1, 25-dihydroxyvitamin D.¹¹ The goal of the treatment of hypoparathyroidism is to maintain serum calcium and phosphorus level in the normal range. Although seizures are common and recurrent in children but most of the time its cause is unknown.¹²

There is limited data on pediatric hypocalcaemia and pediatric hypocalcaemic convulsions in Pakistan. A study from Lahore found 41 (68%) children had hypocalcaemia who presented with afebrile seizures.¹³ Therefore, this study has been planned to evaluate the frequency of hypocalcaemia among infants aged 2 to 60 months presented with afebrile fits. If in this study, hypocalcaemia is found frequent, it will be recommended that calcium levels should be screened and managed immediately among patients having afebrile fits.

Methodology:

Operational Definitions:

Afebrile Fits: Children with presentation of fits (paroxysmal time limited change in motor activity and behavior that result from abnormal electric activity in the brain) without evidence of fever (temperature < 99.5 0F).

Hypocalcaemia: Total serum calcium concentration < 2.1 mmol/L (8.5 mg/dL).

This Cross – sectional study was conducted at Pediatric Department of Liaquat University of Medical and Health Sciences, Jamshoro, with Non probability consecutive sampling technique from February to August-2020.

Total 130 children were included, by sample size calculator (Rao soft Software) by using the proportion as 68% hypocalcemic patients of afebrile fits,¹³ with 95% confidence level and 8% margin error. Permission was taken from the College of Physician and Surgeon Pakistan.

Children of both genders, aged 2 to 60 months presenting with afebrile fits having Birth weight of more than 2.5 kg were included in the study. Children with febrile fits or having the history of diarrhea were excluded.

Written consent was taken from all the parents and all the information was kept confidential after taking fully history, detailed examination. In case of ongoing seizures, oxygen was given and after maintaining the intravenous line, injection diazepam (0.2 mg/kg) was administered. Two ml of blood sample was taken from each patient and was referred to diagnostic laboratory of Liaquat University of Medical and Health Sciences, to observe the calcium levels. In case of proven hypocalcemia, injection calcium gluconate 100mg/kg was given. Other qualitative variables like gender, socioeconomic status, poor sun exposure, malnutrition and anemia were recorded.

Data was analyzed using SPSS version 20.0. Mean and standard deviation were calculated for quantitative variables like age and calcium level. Frequency and percentage were computed for qualitative variables like gender, socio economic status, poor sun exposure, low birth weight, nutritional status, maternal anemia and hypocalcemia. Effect modifiers like age, gender, malnutrition, anemia, educational status, socioeconomic status and number of fits, duration of the fits were controlled through stratification. Chi square test was applied taking p value < 0.05 as significant.

Results:

Majority of the patients, 69 (53.1%) were male, 64 (49.2%) less than or equal to 12 months of age, 28 (21.5%) had maternal educational status as illiterate, 78 (60.0%) belonged to rural areas, 59 (45.4%) belonged to middle socioeconomic status, 69 (53.1%) had poor exposure to sunlight, 80 (61.5%) had malnutrition, 79 (60.8%) with less than 5 episodes of fits per day and 88 (67.7%) had duration of fits per day as less than 5 minutes (As shown in Table 1, 2).

In a total of 130 patients studied, mean age was noted to be 18.36±5.1 months. Overall, mean calcium levels among study cases were noted to be 2.9±0.6 mmol/L while frequency of hypocalcaemia was noted in 81 (62.3%) cases (As shown in Table 1, 2). Stratification of Hypocalcaemia with respect to demographic characteristics is defined in table 3.

When stratification of study variables was done with respect to presence of absence of hypocalcaemia, poor sunlight exposure (p value=0.0011), malnutrition (p value=0.0024) and presence of maternal anemia (p value=0.0094) turned out to be significantly associated with hypocalcaemia while all other study variables were noted to have insignificant association (p value>0.05) with hypocalcaemia (As shown in Table 4).

Table 1: Descriptive characteristics of study participants (n = 130)

Characteristics	Number	Percentage
-----------------	--------	------------

Male	69	53.1
Female	61	46.9
Age (Months)		
<12	64	49.2
>12 to 36	38	23.8
>36 to 60	28	21.5
Area of Residence		
Rural	78	60.0
Urban	52	40.0
Exposure to Sunlight		
Poor (< 30 minutes)	69	53.1
Good (>30 minutes)	61	46.9
Malnutrition		
Yes	80	61.5
No	50	38.5
Maternal Anemia		
Yes	56	43.1
No	74	56.9

Table 2: Hypocalcemia, number and duration of fits in study participants (n = 130)

Characteristics	Number	Percentage
Number of Fits per Day		
<5	79	60.8
≥5	51	39.2
Duration of Fits (minutes) per day		
< 5	88	67.7
≥5	42	32.3
Hypocalcemia		
Yes	81	62.3
No	49	37.7

Table 3: Stratification of Hypocalcaemia with respect to demographic characteristics

Gender	Hypocalcemia		P - value
	Yes (n = 81)	No (n = 49)	
Male	45 (55.6%)	24 (49.0%)	0.4666
Female	36 (44.4%)	25 (51.0%)	
Age Groups (months)			
<12	39 (48.1%)	25 (51.0%)	0.9250
>12 to 36	22 (27.2%)	16 (32.7%)	
>36 to 60	16 (19.8%)	12 (24.5%)	
Residential Status			
Rural	45 (55.6%)	33 (67.3%)	0.6619
Urban	32 (44.4%)	20 (32.7%)	
Socioeconomic status			
Poor	30 (37.0%)	19 (38.8%)	0.8904
Middle	38 (46.9%)	21 (42.9%)	
High	13 (16.0%)	9 (18.4%)	

Table 4: Stratification of Hypocalcaemia with respect to various factors

Exposure to Sunlight	Hypocalcemia		P - value
	Yes (n = 81)	No (n = 49)	
Poor (<30 minutes)	52 (64.2%)	17 (34.7%)	0.0011
Good (>30 minutes)	29 (35.8%)	32 (65.3%)	
Malnutrition			
Yes	58 (71.6%)	22 (44.9%)	0.0024
No	23 (28.4%)	27 (55.1%)	
Maternal Anemia			
Yes	42 (51.9%)	14 (28.6%)	0.0094
No	39 (48.1%)	35 (71.4%)	
Number of Fits per Day			
<5	50 (61.7%)	29 (59.2%)	0.7734
≥5	31 (38.3%)	20 (40.8%)	
Duration of Fits (minutes) per Day			
<5	55 (67.9%)	33 (67.3%)	0.9477
≥5	26 (32.1%)	16 (32.7%)	

Discussion:

In our study, Mean age of the patients was noted to be 18.36±5.1 months while most (49.2%) of the children were below 1 year of age. Our results are different from a local study in which 45 (52.98%) children were males and 40 (47.1%) were females and the mean age was 10.5824 ± 6.84907 months. The hypocalcemic seizures were present in 21 (24.7%) children.¹⁴ The difference in results may be due to age factor, in their study mean age of children was lower than over study participants. In this study, most of the children, 69 (53.1%) were male while no statistical difference in gender was noted. A local study had the similar study participants ie 40 (57.89%) males, total 60 (79%) children were hypocalcemic.¹⁵

In the present study 81 (62.3%) patients with afebrile fits were found to have hypocalcaemia. Hypocalcaemic seizures may present like ‘simple febrile seizures’ that’s why blood tests may be warranted, although most of the time typical simple febrile convulsions are not investigated. In a British study nearly 20% had seizures which satisfied criteria for a ‘simple febrile seizure’ but they were also hypocalcemia.¹⁶ In a similar local study frequency of hypocalcaemia in children presenting with afebrile seizures was 66.48 % (n=56).¹⁷

Sunlight-dependent cutaneous synthesis is the major mechanism for absorption of vitamin D in humans. More specifically, previtamin D3 is nonenzymatically synthesized in the skin from 7-dehydrocholesterol during exposure to ultraviolet light.¹⁸ Lack of sun exposure can cause vitamin D deficiency, leading to hypocalcemic seizures.

We noted poor sunlight exposure, malnutrition and presence of maternal anemia to be associated with the presence of hypocalcaemia among study cases. The results of a local study were similar to our study in which Hypocalcemia was observed in 68.3% cases. Common risk factors were

poor sun exposure (68.3%), malnutrition (61%), low birth weight (54%), while maternal risk factors were, anemic mothers (63.4%), and < 2 year child spacing (51.2%).¹³

Conclusion:

Frequency of hypocalcaemia is very higher in children presenting with afebrile seizures aged 2 to 60 months. Poor exposure to sunlight, malnutrition and presence of maternal anemia were noted to be significantly associated with hypocalcaemia. Studies are needed to further establish whether controlling hypocalcaemia can reduce the risk of seizures or not in the affected children

Approval:

It was taken from the ethical review committee of institute.

Consent:

It was taken from the parents of children

References:

1. Leung AK, Hon KL, Leung TN. Febrile seizures: an overview. *Drugs in context*. 2018; 7.
2. Perucca P, Scheffer IE, Kiley M. The management of epilepsy in children and adults. *Medical Journal of Australia*. 2018; 208(5):226-33.
3. Catarina Franco A, Parreira S, Bentes C, Pimentel J. Management of a first unprovoked epileptic seizure in adolescence and adulthood. *Epileptic Disorders*. 2021; 23(4):537-51.
4. Hauser WA, Beghi E. First seizure definitions and worldwide incidence and mortality. *Epilepsia* 2008;49:8-12
5. Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. *Epilepsia* 1993;34(3):453-68

6. Michoulas A, Farrell K, Connolly M. Approach to a child with a first afebrile seizure
BCMJ 2011; 53:274-7.
7. Kim YO. Benign Convulsions with Mild Gastroenteritis. *Annals of Child Neurology*.
2020 Jan 23; 28(1):2-7.
8. Kawano N, Itonaga T, Tojigamori M, Daa T, Ihara K. A Japanese infant presenting with
hypocalcemic seizures resulting from hypovitaminosis D induced by non-celiac gluten
sensitivity. *Clinical Pediatric Endocrinology*. 2021; 30(2):105-10.
9. Mannstadt M, Bilezikian JP, Thakker RV, Hannan FM, Clarke BL, Rejnmark L, Mitchell
DM, Vokes TJ, Winer KK, Shoback DM. Hypoparathyroidism. *Nature Reviews Disease
Primers*. 2017; 3(1):1-21.
10. Bikle D. Vitamin D: production, metabolism, and mechanisms of action. 2015
11. Khan M, Sharma S. Physiology, parathyroid hormone (PTH). 2018
12. Martin ET, Kerin T, Christakis DA, Blume HK, Gospe SM, Vinje J, et al. Redefining
outcome of first seizures by acute illness. *Pediatrics*. 2010;17:2010
13. Khan MA, Iqbal SM, Afzal MF, Sultan MA. Frequency of hypocalcemic fits in children
presenting with afebrile seizures and risk factors for hypocalcemia: a descriptive study.
Ann King Edward Med Uni 2011; 17(1):31.
14. Rahman, W., Lohana, H., Urooj, S., Ahmed, S., Moeed, A. and Humayun, K., 2020.
Frequency of Hypocalcemic Fits in Children 2 Months to 2 Years of Age, Presenting
with the First Episode of Afebrile Seizures at Hospital Settings in Urban Pakistan: A
Cross-Sectional Study. *Open Journal of Pediatrics*, 10(3), pp.411-422.
15. Abbasi MA, Rajput MS, Zeba N, Lighari JH, Shaikh AA. Frequency of Hypocalcemic
Fits & It's Outcome: An Experience at Tertiary Care Hospital of Sindh. *Journal of*

Peoples University of Medical & Health Sciences Nawabshah. (JPUMHS). 2017;
7(3):110-3.

16. Julies P, Jacobs B. Hypocalcaemic convulsions due to vitamin D deficiency may masquerade as simple febrile convulsions. *Archives of Disease in Childhood*. 2011;96(Suppl 1):A68
17. Rehman M, Bajwa FE, Mushtaq MA, Sarwar I, Amir S, Nawaz R. AFEBRILE SEIZURES. *The Professional Medical Journal*. 2019; 26(05):836-40.
18. Mantadakis E, Deftereos S, Tsouvala E, Thomaidis S, Chatzimichael A. Seizures as initial manifestation of vitamin D-deficiency rickets in a 5-month-old exclusively breastfed infant. *Pediatrics & Neonatology*. 2012; 53(6):384-6.