

Hypocalcemia in Children Presenting with Afebrile Seizures

IRAM NAZ¹, HAFIZ MUHAMMAD MUAZ NAEEM², SUNDAS IKRAM³, MARINA NAZ⁴, MUHAMMAD USMAN⁵, ABDUL REHMAN⁶

¹Senior Registrar Pediatrics, Ghurki Trust Teaching Hospital Lahore

²Senior Registrar Pediatrics, Central Park Teaching Hospital, Lahore

³Consultant ER, Child Life Foundation Children's Emergency Mayo Hospital, Lahore

⁴Senior Registrar Pediatrics, UOL Teaching Hospital, Lahore

⁵Senior Registrar Pediatrics, The Children's Hospital & University of Child Health Sciences, Lahore

⁶Senior Registrar Pediatrics, Pediatric Medicine Unit-1, Mayo Hospital, Lahore

Correspondence to: Iram Naz, Email: Inaz08@gmail.com

ABSTRACT

Objective: To record frequency of hypocalcemia in children presenting with afebrile seizures.

Methodology: This research includes 333 cases presenting with afebrile seizure for evaluation of hypocalcemia at Ghurki Trust Teaching Hospital Lahore during the year 2018. Each child was investigated for serum calcium. Specimen was collected from antecubital fossa by clean venipuncture using sterile disposable syringe. It was immediately transferred to a clean container with cap and sent to laboratory for analysis.

Results: Age range in this study was from 2 months to 7 years with mean age of 3.627±1.68 years, mean duration of seizure 12.864±4.69 hours and mean weight was 16.099±4.44 Kg, 68.2% patients were of male gender and 31.8% patients were females.

Conclusion: Hypocalcemia is a key etiological component in afebrile seizures in infants and children.

Keywords: Children, afebrile seizure, hypocalcemia

INTRODUCTION

Four to seven percent of newborns and toddlers have a seizure at some point.¹ Hypocalcaemia is a significant biochemical aetiology of infantile seizures in low-income nations. Hypocalcemic seizures² may be brought on by a variety of conditions, including preterm, birth asphyxia, an exogenous phosphate load, magnesium shortage, hypoparathyroidism, malabsorption syndromes, pancreatitis, hypoalbuminemia (pseudohypocalcemia), and vitamin D deficiency.³ In impoverished nations, infantile seizures are often caused by hypocalcemia (total serum calcium 8mg/dl) because to vitamin D insufficiency.⁴ The rapid skeletal development of infants makes them a high-risk group for nutritional deficiencies.

Hypocalcemia is related with poor outcome, as evaluated by either survival or duration of critical care stay, making it imperative that calcium levels be maintained at normal levels.⁵ Most of the vitamin D we need is obtained by even brief exposure to sunshine during everyday activities; hence, sunlight also plays a significant role in maintaining calcium homeostasis.⁶ Babies who drink buffalo/cow milk or formula with a lot of phosphate tend to have hypocalcemia as well.⁷ Hypocalcemia risk factors have been identified thanks to both global and regional investigations. Researchers⁸ in India found that low vitamin D levels in mothers, staying indoors during the day, dwelling in metropolitan regions with tall buildings, and sunscreen usage were all significant contributors to this problem. In Pakistan, the research by Khan et al⁹ identified fresh unfortified milk, a lack of sun exposure, a lack of maternal education, and a high family size as potential causes of hypocalcemia.

In a study by Manzoor Ali Khan, it is showed that frequency of hypocalcemia was 68.3% in children presenting with afebrile seizures.¹⁰ There is very limited data on this subject in our local population, only one study has been found so far in Pakistan. Moreover this study was conducted on small sample size of 60 children, so, the results cannot be generalized on all population. Therefore I have planned to conduct this study on large sample size of 333 in our local population. Result of my study will pave the way for further research in this topic and will help to include hypocalcemia screening in routine investigation of children presenting with afebrile seizures

METHODOLOGY

In this study, a total of 333 patients of age two months to seven years male/female presenting with afebrile seizures(children presenting with seizures lasting for > 1 min in the absence of fever temperature) were included in the study, whereas all known cases of epilepsy, known cases of cerebral palsy and brain

malformations or already received calcium treatment on medical record were excluded from this study. Basic demographics (age, gender, duration of seizures) was noted. Each child was investigated for serum calcium. Specimen was collected from antecubital fossa by clean venipuncture and preserved for lab evaluation. All the specimens were collected by 3rd year post graduate resident. Data was recorded and noted by researcher herself in especially designed proforma. Hypocalcemia (total serum calcium <8mg/dl) was recorded and managed as per hospital protocol.

RESULTS

Age range in this study was from 2 months to 7 years with mean age of 3.627±1.68 years, mean duration of seizure 12.864±4.69 hours and mean weight was 16.099±4.44 Kg, 68.2% patients were of male gender and 31.8% patients were females. Hypocalcemia was observed in 62.5% patients.

Table 1: Hypocalcemia in Children Presenting with Afebrile Seizures (n=333)

Variables		Hypocalcemia		P value
		Yes	No	
Age	2 months to 3 years	91(60.3%)	60(39.7%)	0.451
	4 to 7 years	117(64.3%)	65(35.7%)	
Gender	Male	135(59.5%)	92(40.5%)	0.099
	Female	73(68.9%)	33(31.1%)	
SES	Low	50(84.7%)	9(15.3%)	0.000
	Middle	154(63.6%)	88(36.4%)	
	High	4(12.5%)	28(87.5%)	
Duration of seizures	1-12 hrs	99(63.1%)	58(36.9%)	0.832
	13-24 hrs	109(61.9%)	67(38.1%)	

DISCUSSION

Our study was designed to determine the frequency of hypocalcemia among patients of afebrile seizures in our setting and to formulate health education programme as well to prevent hypocalcemia and its related morbidities e.g. seizures. Hypocalcemia is one of the most prevalent metabolic abnormalities and a treatable cause of seizures. Seizures are widespread in children and adolescents, and this age group is prone to having them. 11 It is possible that a lack of understanding of the morbid effects of hypocalcemia is contributing to the fact that the condition is becoming more widespread, so, our limited effort was meant to reveal magnitude of hypocalcemic seizures in afebrile patients.

In our study, total 333 patients of afebrile seizures were included, out of these, 208 (62.5%) cases were found to be

hypocalcemic. Total male patients were 68.2 % while females were 31.8 % but this difference was not statistically significant (p -value=0.09). Among these 333 patients, 91 (60.3%) were between 2 months to 3 years and 117 (64.3%) were between 4 to 7 years but this difference was again not statistically significant (p -value=0.4).

In a study by Manzoor Ali Khan, it is showed that frequency of hypocalcemia was 68.3% in children presenting with afebrile seizures.¹⁰ In their study, common age group consisted of children <6 months while in our study mean age was 3.627 ± 1.68 years. This difference was because of different inclusion criteria in both studies. In their study age range was from 2 months to 2 years while in our study it was from 2 months to 7 years.

The mean age at time of admission was 3.627 ± 1.68 years. This is in contrast with results of study done by Abanamy et al.¹⁴ Their study showed 39.2% patients less than 6 months of age and 14.2% younger than 3 months of age. This most probably relates to maternal vitamin D deficiency.

Present study noted male predominance (68.2%) comparable with Binmohana MA et al,¹³ in their study 60% of patients were males and 40% were females. Abanamy et al¹⁴ also showed male predominance of 64.4 % but Sharma et al¹⁵ found no sex difference.

Study done by Sharma et al¹⁵ showed that 23 % of hypocalcemic children presented with convulsions. Inadequate exposure to sunlight is a significant factor related with the development of vitamin D-deficient rickets, which is, in turn, a frequent cause of hypocalcemia in children. Rickets is characterised by abnormally soft and brittle bones.¹²

Abanamy et al¹⁴ also showed that children do not get enough exposure to sunlight due to local factors like housing designs and clothing styles. Major factor is that parents have strong tendency to avoid sun exposure and heat.

Binmohana et al¹³ also reported that prevalence of hypocalcemia was 58% which is also close to our results. Patients with hypocalcaemic afebrile fits are common in urban referral hospitals in underdeveloped nations. Lack of calcium and other micro and macronutrients have been linked to hypocalcaemia, as proven by Cetinkaya.¹⁷⁻¹⁹ Researchers Humayun et al. found that poor socioeconomic status, low maternal education, limited exposure to sunshine, and big family size are all significant risk factors for vitamin D deficiency, which may cause hypocalcemic seizures and other complications.

In another study done by Mantadakis et al,⁴ it is shown that seizures were initial manifestation of hypocalcemia in infants. Reason behind was vitamin D deficiency rickets due to poor sun exposure. Chisti MJ et al² in Bangladesh shown that severely malnourished children presenting with hypocalcemia were having increased risk of convulsions and fatal outcomes like death than those without hypocalcemia. So, we should take preventive measures, like calcium supplementation, in addition to other aspects of management of seizures.

We showed relation of hypocalcemia with seizures while, in their study, Steele T et al⁵ showed that hypocalcemia in early course of critical illness is also associated with increased mortality.

In another study, conducted by Khan HI et al,⁹ it is shown that hypocalcemia is major health problem in Pakistani children. It can present with wide variety of symptoms, the most important of which are seizures and recurrent chest infections. They showed that, major cause of vitamin D deficiency and hypocalcemia in children under 2 years of age was either exclusive breast feeding or use of fresh milk without adequate sun exposure. Our study also showed that hypocalcemia was underlying etiology in 62.5% of patients presenting with afebrile seizures.

This research examined hypocalcaemic fits as a cause of feverless fits. This research helps us understand the burden of calcium and vitamin D supplementation and establish future benchmarks. Although our research is limited due to limited resources and time but hypocalcemia should be anticipated

,investigated and treated adequately to prevent morbidities inclusive of afebrile seizures which can ultimately lead to fatal outcomes.

CONCLUSION

This research concludes that hypocalcemia is a key etiological component in afebrile seizures in infants and children. Less sun exposure, feeding infants unfortified animal milk, delayed weaning, maternal anaemia, maternal age, multiparity, and smaller intervals between births are all major contributors to this risk. Hypocalcemia may be averted, greatly reducing morbidity from hypocalcemic fits and rickets, by raising awareness about these risk factors in the general population. Therefore, the likelihood that a mother's offspring would be hypocalcemic decreases with the mother's degree of education.

REFERENCES

1. Assogba K, Balaka B, Touglo FA, Apetsè KM, Kombaté D. Febrile seizures in one-five aged infants in tropical practice: frequency, etiology and outcome of hospitalization. *J Pediatr Neurosci.* 2015;10(1):9-12.
2. Chisti MJ, Salam MA, Ashraf H. Prevalence, clinical predictors, and outcome of hypocalcaemia in severely-malnourished under-five children admitted to an urban hospital in Bangladesh: a case-control study. *J Health Popul Nutr.* 2014;32(2):270-5.
3. Ahmed A, Azim A, Gurjar M, Baronia AK. Hypocalcemia in acute pancreatitis revisited. *Indian J Crit Care Med.* 2016;20(3):173-7.
4. 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. *Pediatr Neonatol.* 2012;53(6):384-6.
5. 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.
6. Wacker M, Holick MF. Sunlight and vitamin D: a global perspective for health. *Dermatoendocrinol.* 2013;5(1):51-108.
7. Martin CR, Ling PR, Blackburn GL. Review of infant feeding: key features of breast milk and infant formula. *Nutrients.* 2016;8(5):279.
8. Balabramanian S, Ganesh R. Vitamin D deficiency in exclusively breast - fed infants. *Indian J Med Res.* 2008;127(3):250-5.
9. 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.
10. Khan MA, Iqbal SMJ, 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):31-5.
11. 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.
12. Binmohana MA, Raja YA, Saif GA. Prevalence of hypocalcemia in children examined for serum calcium in Sana'a, Yemen. *Saudi Med J* 2005; 26: 457-9.
13. Abanamy A, Salman H, Cheriyan M, Shuja M, Siddrani S. Vitamin D deficiency Ricket in Riyadh. *Ann Saudi Med* 1991; 11: 35-9.
14. Sharma A, Virmani DN. Ricket in wall city of Dehli. *Indian Paediatr* 2004; 41 (10): 1076-1.
15. 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.
16. Egri C, VilinYY, Ruben PC. Thermoprotective role of the sodium channel $\beta 1$ subunit is lost with the $\beta 1$ (C121W) mutation. *Epilepsia* 2012;53(3):494-505.
17. Radzicki D, YauHJ, Pollema-Mays SL. Temperature-sensitive 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.
18. Salam SM, Rahman HM, Karam RA. GABRG2 gene polymorphisms in Egyptian children with simple febrile seizures. *Indian J Pediatr* 2012;79(11):1514-6.
19. Aicardi J. *Epilepsy in Children.* 1994 New York, NY: Raven Press.
20. Aicardi J. Syndromic classification in the management of childhood epilepsy. *J Child Neurol.* 1994; 9(suppl):2S14-2S18.