



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

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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 $\leq 99.6^{\circ}\text{F}$) 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 \pm 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 \pm SD = 23.28 ± 12.56 months

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

Sun exposure	No. of Patients	%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.

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

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

<i>socioeconomic status</i>	<i>Hypocalcaemia</i>	
	Present	Absent
<i>Poor</i>	06	33
<i>Middle</i>	09	45
<i>High</i>	00	13
<i>P-value</i>	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, delevated 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 hypocalcemia.^{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 clonic which was comparable with Sharma et.^{xxxiv} 53.3% of patients had elevated alkaline phosphatase > 1000 IU/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.

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