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Original Article

Serum Calcium Level among Children with Simple Febrile Seizures Admitted in Chittagong Medical College Hospital

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Abstract

Background: *Febrile seizure is one of the most common form of seizure occurring in children. Water and electrolyte imbalance occur during acute febrile illness and hypocalcaemia is one of them. It has been found that change in serum calcium might enhance the susceptibility to seizure. This study is aimed to evaluate the association of serum calcium level and febrile seizure among hospitalized children.*

Materials and methods: *This cross-sectional case control study was conducted among 100 hospitalized children of febrile illness in Department of Paediatrics of Chittagong Medical College Hospital, Chattogram, Bangladesh from June 2022 to November 2022. Febrile patients of 6- 60 months of age were enrolled during this study period in two groups, one with seizure and another without seizure. Serum calcium was measured by automated biochemistry analyzer, in a method of Arsenazo-III photometry principle. Collected data were classified, edited, coded and entered into the computer for statistical analysis by using SPSS v23. Statistical significance was defined as p < 0.05 and confidence interval level was set at 95%.*

Results: *The mean age was 20.3±13.1 months in case group and 18.0±12.7 months in control group. Overall male patients were predominant, 29(58.0%) and 30(60.0%) in case and control group respectively. Age, sex, religion, residence and gestational age were not comparable in two groups. The difference of mean birth weight was statistically significant between two groups, 2176.0±293.1 grams in case group and 2328.0±249.9 grams in control group. Most (96.0%) of the patients developed seizures within 7-12 hours of onset of fever. Duration of seizure was 6-10 minutes in half of the patients. Generalized tonic clonic seizure was found to be the predominant seizure type (96%). Cough and cold as presenting features were more in control group than case group (78.0% vs 46.0%). Hypocalcaemia (<8.8 mg/dl) was found significantly higher in case group (50.0% vs 10.0%) with OR (9.0 and 95% CI 3.06-26.44%).Higher mean serum calcium level was significantly documented in control group (8.8±0.9 mg/dl vs 9.4±0.5 m/dl in case and control group respectively).*

Conclusion: *Significant association was found between serum calcium levels and the occurrence of febrile seizures. Low serum calcium levels and occurrence of febrile seizure showed significant association. Presence of low serum calcium levels of less than 8.8 mg/dl was more in patients with febrile seizure.*

Key words: Febrile seizures; Hypocalcaemia; Serum calcium level.

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INTRODUCTION

Seizure is one of the important paediatric health problems in developing and developed countries and febrile seizure is the most common seizure disorder in childhood, affecting 2% to 5% of children between the ages of 6 and 60 months.[1] It is generally believed that Febrile Seizure (FS) is an age-dependent response of the

immature brain to fever.[2] Despite its benign nature, the febrile seizure is one of the most common reason for admission to pediatric emergency worldwide.[3]

The exact pathogenesis of febrile seizure is not fully understood but involves several factors like genetic predisposition, changes in neurotransmitters level and some trace elements. [4-5] A common biochemical abnormality causing seizure is hypocalcemia, which may also manifest as muscle cramps, tetany and paraesthesia. During any acute febrile disease, disturbances in water and electrolytes occurs frequently. It has been suggested that change in serum calcium might enhance the susceptibility to seizure.[6] The basic physiology of a seizure episode is detected in an unstable cell membrane or its surrounding supportive cells.[7] The seizure originates from the grey matter of any cortical or subcortical area.[8] Reduced serum calcium causes increased neuroexcitability. Low ionized calcium level in the extracellular fluid, by binding to the exterior surface of the sodium channel protein molecule in the plasma membrane of nerve cells, increases the permeability of neuronal membranes to sodium ions, causing a progressive depolarization thus increases the possibility of action potentials. When Calcium ions are absent, the voltage level required to open voltage gated sodium channels is significantly altered (Less excitation is required). With hypocalcemia, action potentials may be spontaneously generated causing contraction of peripheral skeletal muscles resulting in clinical seizure.[9]

Various studies of different countries show significant association between serum calcium and febrile seizure. [10,11] A clear understanding of association of serum calcium level with febrile seizure will be helpful for therapeutic and preventive purpose during such case management. This test is cheap, can be easily done in many institutes, inference of which may further help both in treatment as well as in counselling and alleviation of parental anxiety. This study is aimed to evaluate the association of serum calcium level and febrile seizure among hospitalized children.

MATERIALS AND METHODS

This case control study was conducted in Department of Paediatrics, Chittagong Medical College Hospital, Chattogram, Bangladesh from June 2022 to November 2022. This study was done after obtaining ethical clearance from the Ethical review Committee. The patients were selected after fulfilling the following inclusion and exclusion criteria.

Inclusion criteria:

Cases

Children of 6 months to 60 months age admitted with febrile seizures.

Control

Febrile children with age between 6 months to 60 months admitted without seizures.

Exclusion Criteria:

- Patients presenting with afebrile seizure
- Febrile seizure patients with hypoglycemia or Hyponatremia
- CNS malformations or CNS infection
- Known case of metabolic disorder
- Unconscious patients.

Fifty children presenting with febrile seizure, fulfilling inclusion criteria were enrolled as cases, along with similar number (Fifty) of age and sex matched controls. Venous blood samples were obtained and calcium serum magnesium levels were done. The results of cases and controls were compared. Data were analyzed through SPSS (Version 25) software. Significance for the statistical tests (Chi Square test and unpaired t-test) were determined at a probability value of less than 0.05 ($p<0.05$).

RESULTS

Table I Socio-demographic characteristics of the study subjects (n=100)

Socio-demographic characteristics	Case (n=50)		Control (n=50)		p value
	n	%	n	%	
Age (Months)					
6-12	21	42.0	25	50.0	
13-24	19	38.0	13	26.0	
25-36	4	8.0	8	16.0	
37-48	4	8.0	2	4.0	
49-60	2	4.0	2	4.0	
Mean±SD	20.3	±13.1	18.0	±12.7	[a]0.378[ns]
Range (Min-max)	6.0	-60.0	6.0	-53.0	
Sex					
Male	29	58.0	30	60.0	[b]0.500[ns]
Female	21	42.0	20	40.0	
Religion					
Muslim	44	88.0	43	86.0	
Hindu	6	12.0	6	12.0	[b]0.603[ns]
Others	0	0.0	1	2.0	
Residence					
Urban	19	38.0	11	22.0	[b]0.081[ns]
Rural	31	62.0	39	78.0	

ns=not significant

[a]p value reached from unpaired t-test

[b]p value reached from chi square test.

Table I shows that about half of the patients were 6-12 months old in both the study groups and no significant difference of mean age was observed .Muslim male patients of rural residence were predominant in both groups.

Table II Birth weight of study subjects (n=100)

Birth weight (grams)	Case (n=50)		Control (n=50)		Difference (95% CI)	p value
	n	%	n	%		
<2500	39	78.0	34	68.0		
2500-4000	11	22.0	16	32.0		
Mean±SD	2176.0	±293.1	2328.0±249.9		-152.0	0.006[s]
Range (Min-max)	1500.0	-2600.0	1600.-2800.0		(-260.1to-43.9)	

s= significant
p value reached from unpaired t-test.

Table II shows that majority of patients in both of the groups born with low birth weight. But mean birth weight of two groups of patients showed significant difference.

Table III Time of starting weaning of the study subjects (n=100)

Weaning started (Months)	Case (n=50)		Control (n=50)		OR (95% CI)	p value
	n	%	n	%		
≤6	3	6.0	0	0.0	-	0.084[ns]
7-9	37	74.0	47	94.0	0.18(0.05 to 0.69)	0.006[s]
>9	10	20.0	3	6.0	3.92 (1.01 to 15.22)	0.037[s]

s= significant, ns=not significant
p value reached from chi square test.

Table III shows that more than 90% patients in control group and less than 75% patients of case groups had appropriate weaning time and the difference was statistically significant. One fifth of the patients in case group had late weaning and it was also found significant when compared with the control group.

Table IV Febrile seizure description of the study subjects (n=50)

	Number of patients	Percentage (%)
Time of seizure from fever (Hours)		
≤ 6	21	42.0
7-12	27	54.0
>12	2	4.0
Average length seizure (Minutes)		
≤ 5	19	38.0
6-10	25	50.0
>10	6	12.0

Table IV shows that more than 95% of the patients of case group developed single attack of seizure within 12 hours of onset of fever. Duration of seizures was typically less than 10 minutes in majority (88%) of patients.

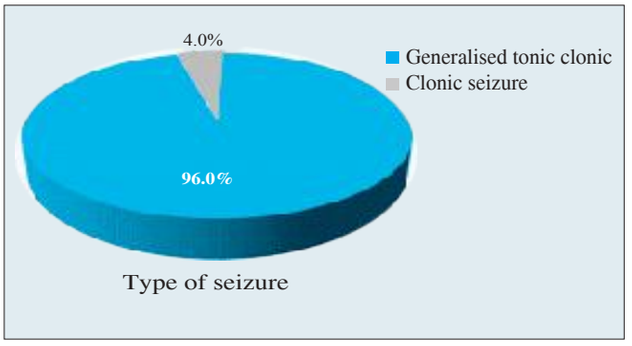

Figure 1 Type of seizure of the study patients (Case group)(n=50)

Table V Presenting complaints at admission of the study subjects (n=100)

Presenting complaints at admission	Case (n=50)		Control (n=50)		p value
	n	%	n	%	
Cough and cold	23	46.0	39	78.0	0.001[s]
Ear discharge	5	10.0	1	2.0	0.102[ns]
Urinary symptoms	6	12.0	3	6.0	0.243[ns]
Vomiting	4	8.0	3	6.0	0.500[ns]
Diarrhoea	2	4.0	1	2.0	0.500[ns]
Abdominal discomfort	5	10.0	4	8.0	0.500[ns]

s=significant ns=not significant
P value reached from chi square test.

Table V shows that significantly higher proportion of patients in control group presented with cough and cold. Other clinical features were not statistically different between the study groups.

Table VI Serum calcium of the study subjects (n=100)

Serum calcium (mg/dl)	Case (n=50)		Control (n=50)		OR (95% CI)	p value
	n	%	n	%		
Hypocalcaemia (<8.8mg/dl)	25	50.0	5	10.0	9.0	
Normal (≥8.8mg/dl)	25	50.0	45	90.0	(3.06-26.44)	[a]0.001[s]
Mean±SD	8.8	±0.9	9.4	±0.5		[b]0.001[s]
Range (Min-max)	5.8	-10.3	8.3	-10.7		

s= significant
ap value reached from Chi square test
bp value reached from unpaired t-test.

Table VI shows that half of the patients in case group and one tenth patients in control group had hypocalcaemia and this difference was statistically significant. The mean serum calcium was found significantly higher in control group.

DISCUSSION

Majority of the patients in this study were 6-12 months old, 21(42.0%) in case group and 25(50.0%) in control group. The

mean age was 20.3±13.1 months in case group and 18.0±12.7 months in control group, the difference was not comparable. Study conducted by Tiwari et al. Sharawat et al. andU shakiran et al. showed same findings consisted with that of the present study. Peak age of incidence was 12 month in this study.[1,3,11]

Present study observed that male patients were predominant in both groups, 29(58.0%) in case group and 30(60.0%) in control group. The difference was not statistically significant (p>0.05). This was similar to the findings (60% and 58% respectively) of a study conducted by Dadhich et al.[6] Another study done by Tiwari et al. also reported male predominance. That means FS affect both male and female equally.[1]

Present study observed that most of the patients in both the study groups born with low birth weight, 39(78.0%) in case group and 34(68.0%) in control group. The mean birth weight was 2176.0±293.1 grams in case group and 2328.0±249.9 grams in control group and this difference was statistically significant. This was similar to the findings of a study conducted by Nishiyama et al.[12] The mean birth weight was 2981±435 g and 3001±421 g in seizure and no seizure group respectively. Such difference was statistically significant (p<0.001). Another study done by Christensen et al. showed that low birth weight child have an overall higher risk of febrile seizure, which also supports the present study.[13] Thus risk of FS increases with decreasing birth weight may be to stage of brain development.

Present study observed that most of the patients in control group started weaning at 7-9 months of age compared to case group, 47(94%) vs 37 (74%) with a OR 0.18. On the other hand, 10 patients (20%) of case group started weaning at > 9 months in comparison with 3 patients (6%) in control group with OR 3.92. Both the differences were statistically significant. That means weaning at appropriate time decreases frequency of febrile seizure whereas late weaning increases febrile seizure.

Present study observed that most (96.0%) of the patients developed seizure within12 hours of onset of fever. All patients had single attack of seizure. Half of the patients had seizure duration of 6-10 minutes. Majority 48(96.0%) patients had generalized tonic clonic seizure. In a study done by Biswas et al. reported that febrile seizures were generalized in 72 (90%) cases and in 70 (87.5%) cases, the duration was less than 15 minutes.[14] Regarding clinical features at admission, it was observed that cough and cold as presenting features were more in control group than case group (78.0% vs 46.0%). Other clinical features were not statistically different between two groups (p>0.05). In a study conducted by Biswas et al. reported that the most common symptoms were cough 31(38.8%) and coryza 25(31.2%) that support the present study.[14]

Present study observed that hypocalcaemia (<8.8 mg/dl) was significantly higher in case group than control group (50.0% vs 10.0%) with OR 9.0 and 95% CI (3.06- 26.44%). The mean serum calcium was 8.8±0.9 mg/dl in case group and 9.4±0.5 mg/dl in control group, that was also significant (p=0.001). Sharma et al. demonstrated that in study group, 12 (24%) patients had abnormal (<4.4 mg/dl) range of calcium level while in control group no patient had abnormal ionized calcium level.[15] Mean calcium level was 4.62±0.26 mg/dl and 4.88±0.27 mg/dl in study and control groups respectively and this difference was found statistically highly significant (p<0.001). Sharawat et al. observed that mean serum calcium level was significantly higher in control group than case group (9.0±0.6 vs 8.2±0.6 mg/dl).[3] In a study by Akbayrams et al. where 48 children with febrile seizures were compared with age matched controls and found low serum calcium (p=0.001).[16] This observation is also similar to studies by Chiarelli et al. where serum calcium level was significantly lower in children with FS.[10] On the other hand, a study conducted by Halkude et al. reported that serum calcium was low in 15 (19.7%) cases and in 29 (38.2%) controls and mean (SD) values were 9.17±0.56 and 8.91±0.75 respectively.[7] Mean value was higher in cases and result was statistically significant (P=0.01). Dadhich et al. reported mean calcium level as 4.52±0.24 mg/dl and 4.01±0.16 mg/dl in control and case groups respectively and this difference was statistically highly significant (p<0.001).[6] There was no association between low Serum calcium and FS in study by Sayedzadeh et al. Naseer et al. Namakin et al. Ushakiran et al.[17-19,11]

LIMITATION

It was as single-centered study with small sample size. Moreover randomization and blinding were not done.

CONCLUSION

Significant association was found between low serum calcium levels and the occurrence of febrile seizures. So from this study it can be concluded that hypocalcemia is a precipitating factor for FS.

RECOMMENDATION

Further follow up study with calcium supplementations of the same FS patients are recommended to validate the study result.

DISCLOSURE

All the authors declared no competing interest.

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