HypomagnesemiaIs a Risk Factor of Febrile Seizure in Children

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Abstract

Background: Febrile seizure is a common pediatric emergency. This is the most common type of seizure in children aged 6 months to 6 years constituting 30% of all seizure types. Despite the high clinical burden of febrile seizure, little advance has been made in understanding its etiology. Magnesium deficiency is fairly common; clinicians rarely test for it in patients with febrile seizure. Hence this study is undertaken to find out whether low serum magnesium level is a risk factor of febrile seizure in children. The objective of the study was to determine the relationship of low serum magnesium level with febrile seizure.

Materials and methods: This case-control study was conducted in Department of Pediatrics, Dhaka Medical College Hospital, Dhaka from January, 2019 to December, 2019. Forty-one children with febrile seizure enrolled as cases, along with similar number (Forty-one) of age and sex matched controls. Venous blood samples were obtained and analyses of 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 & unpaired t-test) were determined at a probability value of less than 0.05 ($p<0.05$).

Results: Mean age of the respondents was 1.78±0.99 years in case and 1.48±0.94 years in control group. Family history of febrile seizure was present in 29.27% of the cases. Hypomagnesemia was noticed in 24.39% children with febrile seizure, on the other hand, 7.31% in controls and the difference was statistically significant. The Odds ratio was 4.08.

Conclusion: serum magnesium was found to be significantly low in children with febrile seizure than that of febrile children without seizure. So, it may be concluded that low serum magnesium level can be regarded as a risk factor of febrile seizure in children. However further large-scale studies are needed to generalize the result of this study.

Key words: Febrile seizure, children, serum magnesium level.

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Submitted on : 04.02.2023
Accepted on : 10.03.2023

Introduction

Febrile seizure is a common emergency in pediatric ward. This is the most common type of seizure in children aged 6 months to 6 years which constitute 30% of all seizure types.[1] A seizure is a transient occurrence of signs and/or symptoms resulting from abnormal excessive or synchronous neuronal activity in the brain. Specially in the children, it is related to specific risk factors like positive family history, fever, infections, neurological comorbidity, premature birth etc.[2]

Currently accepted definition of febrile seizure is, "febrile seizures are seizures that occur between the age of 6 and 60 months with a temperature of 38°C (100.4°F) or higher, that are not the result of central nervous system infection or any metabolic imbalance, and that occur in the absence of a history of prior afebrile seizures".[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 like copper, zinc and magnesium.[4] There are different hypotheses about change in neurotransmitters and trace elements level which can have a role in the pathogenesis of febrile seizure. Several factors such as vitamin B6 deficiency, electrolyte disturbances, reduction in serum zinc, selenium, and magnesium levels and low Gamma-Aminobutyric Acid (GABA) levels are believed to play a role in the pathogenesis of febrile seizure.[5]

Magnesium is the fourth most common cation in the body and the third most common intracellular cation.[6] Mechanism of seizure due to hypomagnesaemia is explained as follows:

i) Hypomagnesaemia causes release of inhibition of voltage dependent gradient at NMDA receptor. This leads to glutamate mediated depolarization of the post synaptic membrane and enhancement of epileptiform electrical activity.[7]

ii) Magnesium acts as a voltage-dependent calcium channel antagonist, thus hypomagnesaemia will lead to release of calcium ions, which causes nerve excitability.[8]

iii) Magnesium affects calcium metabolism as the production of cyclic Adenosine Monophosphate (cAMP) is magnesium dependent, which in turn controls the release of parathyroid hormone.[6,7]

Mg is necessary for maintaining normal neurological function and neurotransmitter release, regulation of muscular contractions or relaxations, parathormone hormone secretion and activity, insulin signal transmission, modulating the immunological functions etc.[9]

Although magnesium deficiency is fairly common, clinicians rarely test for it in patients with febrile seizure. Hence the study is undertaken to find out whether low serum magnesium level is a risk factor of febrile seizure in children. To determine the relationship of low serum magnesium level with febrile seizure.

Materials and methods

This case-control study was conducted in department of Pediatrics, Dhaka Medical College Hospital, Dhaka from January, 2019 to December, 2019. The 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:

i) Children with febrile seizure with age between 6 months to 5 years.

ii) Sex: Both

Controls:

i) Age and sex matched children

ii) Fever (<7 days) without seizures

Exclusion criteria

i) History of afebrile seizure
ii) History of neonatal seizures
iii) Suspected CNS infections
iv) Suspected neurometabolic disorders
v) Severe acute malnutrition
vi) Receiving magnesium supplementation.

Forty-one children presenting with febrile seizure, fulfilling inclusion criteria were enrolled as cases, along with similar number (Forty-one) of age and sex matched controls. Venous blood samples were obtained and analyses of 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 Distribution of the study subjects by age& sex (n=82)

	Case (n=41)		Control (n=41)		p value
Age (Years)	n	%	n	%	
<1	7	17.07	11	26.83	
1 to <2	19	46.34	21	51.22	
2 to <3	7	17.07	5	12.12	
3 to <4	6	14.63	1	2.45	
4 to 5	2	4.87	2	4.87	
Mean±SD	1.78±0.99		1.48±0.94		0.16^{ns}
Sex					
Male	27	65.85	25	60.97	0.647^{ns}
Female	14	34.15	16	39.03	

ns= not significant.
p value reached from unpaired t-test.

Table II Characteristics of seizure in cases (n=41)

	Case (n=41)	
Types of seizure	n	%
Generalized	41	100
Focal	0	0.0
Duration (Minutes)		
≤15	38	92.7
>15 to <30	0	0.0
≥30	3	7.3
Mean ±SD	8.87±7.09	
Range (Min-max)	2 to 30	
Types of febrile seizure		
Simple febrile seizure	38	92.7
Complex febrile seizure	0	0.0
Febrile status epilepticus	3	7.3

Table III Serum magnesium level of the study subjects (n=41)

Serum magnesium (mg/dl)	Case (n=41)		Control (n=41)		Odds Ratio (OR)	p value
	n	%	n	%		
Hypomagnesemia (<1.5 mg/dl)	10	24.39	3	7.31	4.08	
Normal	31	15.61	38	92.68		
Mean±SD (mg/dl)	2.09±0.60		2.33±0.43			0.043[s]
Range (Min-max)	1.08	-3.00	1.35	-3.10		

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

Discussion

In this study, 46.34% of cases and 51.22% of controls were between 1 to 2 years of age. The mean age was 1.78±0.99 years in cases which is similar to another study conducted in Bangladesh where mean age was 1.6±0.34 years.[10] Some studies showed mean age of febrile seizure lies between 2 and 2.5 years of age.[11-14] But another study done in Bangladesh by Biswas et al. found that 51.25% of 80 cases were between 6 to 12 months of age.[15]

In this study majority of the cases (65.85%) were male and male female ratio was 1.9:1. This difference was not statistically significant. Mollah et al. in Bangladesh also showed that male children were more prone to febrile seizure than female children and male female ratio was 1.78:1.[10] Begum et al. found male female ratio was 1.5:1.[18] Other studies also showed male predominance[7,11].

In current study all the children with febrile seizure had GTCS (100%) which is same (100%) to study done by Baek et al.[12] This is almost similar (90%) to another study done in Bangladesh to Bharathi et al. in their study found that 51 (42.5%) of 120 cases had GTCS.[16,7] In this study mean duration of seizure was 8.87±7.09 minutes and in majority (92.7%) of cases, duration of seizure was ≤15 minutes. This is similar to another study where 87.5% of cases had seizure <15 minutes.[16] In the study done by Baek et al. mean duration of seizure was 2.37±2.20 minutes.[14]

Serum magnesium level was found significantly low in cases than the controls. Hypomagnesemia was noticed in10 (24.39%) children with febrile seizure. To the contrary, 3 (7.31%) of the controls were with low serum magnesium level and this difference is statistically significant ($p<0.05$). Nemichandra et al. found 17.1% and Bharati et al. found 16% of children with febrile seizure had hypomagnesemia which was statistically significant.[11,7] Study done by Baek et al. showed that 57 (42.9%) out of 133 cases of febrile seizure had hypomagnesemia.[12] In another study conducted in India, serum magnesium level was low in 32% cases with febrile seizure.[17] Several other studies also showed hypomagnesemia is related with febrile seizure.[4,13] In this study Odds Ratio was 4.08. So low serum magnesium level is a risk factor of febrile seizure in children. Baek et al. also found that hypomagnesemia was an independent risk factor for developing febrile seizure.[12]

Limitation

This study has been conducted in a single centre with small sample size in a single tertiary care hospital.

Conclusion

From the result of this study, it can be concluded that serum magnesium is significantly low among the children with febrile seizure compared to febrile children without seizure. So, hypomagnesemia can be regarded as a risk factor of febrile seizure in children.

Recommendation

The study finding might lack the power to become generalizable in large scale and may not represent the whole population of our country.

Acknowledgement

The authors express their gratefulness to all patients and their guardian those who are participated in the study.

Contribution of authors

MMH-Conception, acquisition of data, drafting & final approval.

DC-Desing, critical revision & final approval.

MJBAC-Acquisition of data, data analysis, drafting & final approval.

SRC-Acquisition of data, drafting & final approval.

ANMTC-Interpretation of data, critical revision & final approval.

PG-Data analysis, critical revision & final approval.

SD-Interpretation of data, critical revision & final approval.

Disclosure

All the authors declared no conflict of interest.

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