



## Study of Association of Serum Magnesium with Febrile Seizures among Children Admitted In Tertiary Care Hospital

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### I. INTRODUCTION

A seizure is transient occurrence of signs and/or symptoms resulting from abnormal excessive or synchronous neuronal activity in the brain.<sup>1</sup>A seizure results when a sudden imbalance occurs between the excitatory and inhibitory forces within the network of cortical neurons.<sup>2</sup>A febrile seizure is the most commonly witnessed seizures type among the paediatric population. **Febrile seizures** are seizures that occur between the ages of 6 months and 60 months with a temperature of 38<sup>0</sup>C(100.4<sup>0</sup>F) or higher, that are not the result of CNS infection or any metabolic imbalance, and that occur in the absence of a history of prior afebrile seizures. Febrile seizures are divided into two types, simple febrile seizure and complex febrile seizure.<sup>3</sup>A **simple febrile seizure** is a primary generalized, usually tonic clonic, attack associated with fever, lasting for a maximum of 15 min and not recurrent within a 24 hrs period. A **complex febrile seizure** is more prolonged (15 min), and/or is focal, and/or recurs within 24 hours. It is the most common seizure in children <60 months, with a peak incidence occurring around 18 months of age.<sup>4</sup>It has been suggested that changes in serum electrolyte levels, might enhance the susceptibility to seizure and its recurrence during a febrile disease in childhood.<sup>5,6,7</sup>Studies have shown that a number of major and trace elements like iron, zinc, selenium, copper, sodium, potassium, calcium and magnesium play a significant role in febrile convulsions by their co-enzyme activity or ability to influence ion channels and receptors.<sup>8,9,10,11,12</sup>Magnesium (Mg) also influences neuronal function by inhibiting facilitatory effect on calcium (Ca) in synapses and thereby inhibiting neuronal transmission and it also blocks a voltage dependent NMDA receptor channel. Thus we studied serum magnesium levels and its associations among the febrile seizure children and compared it with controls in a tertiary care hospital of western Maharashtra.

### Role of Magnesium

The 4<sup>th</sup> most common cation in the human body is magnesium. It is also the 3<sup>rd</sup> most common cation intracellularly. The bone has major share of magnesium in our body, which accounts for 50-60% of magnesium in our body. But, most of the intracellular magnesium is protein bound; only 25% of it is in the exchangeable form. Intracellular magnesium is in the liver and muscles where metabolic rate is high. Magnesium is also essential for membrane stability and nerve conduction.<sup>13</sup>Magnesium has the capacity to block NMDA receptor and also inhibits the role of calcium in synaptic transmission. Low serum magnesium has occasionally been associated with significant effects on the central nervous system especially in epilepsy.<sup>14</sup>

### II. MATERIALS AND METHODS

**Type Of Study-** Analytical study

**Study Design-** Case Control Study

**Study Subjects-** Children with fever admitted to hospital aged 6 months to 60 months. Children with febrile seizures were taken as cases and febrile children without seizure were taken as controls.

**Study Period-** 2 years

**Sample Size Calculation:**

Considering the Prevalence / proportion of febrile seizures among children of 6 months to 60 months as 5% with marginal error of 5% and under 95% confidence interval

$N = \frac{4pq}{e^2}$

**N= Sample size**

**P= Prevalence of febrile seizure Q= 100-P**

**E= Marginal error**

**After substituting the values, the sample size comes to 76 in each group**

**Data Collection -** At the beginning of the study, the data collection was done on the basis of subjects (cases and controls) admitted in the wards who were fulfilling the inclusion criteria of the study and after written informed consent was obtained from the guardian/parent. The selected study subjects'



(cases and controls) detail information was collected from the guardian /parent as per the proforma (Demographic information, History,

General and Physical examination). Blood samples were collected and sent for their investigations.

**Inclusion Criteria And Exclusion Criteria**

<b>INCLUSION CRITERIA</b>	<b>EXCLUSION CRITERIA</b>
<b>Cases</b>	<b>Cases</b>
<ul style="list-style-type: none"> <li>Children with age between 6 months to 60 months with febrile seizures</li> </ul>	<ul style="list-style-type: none"> <li>Children with seizures due to central nervous system infections</li> <li>Children with past medical history of seizures of any other etiology</li> <li>Children with CNS malformations, Developmentally challenged</li> <li>Children on micronutrient supplements</li> <li>Children with metabolic disorder, cardiac, kidney disease, gastroenteritis</li> </ul>
<b>Control</b>	<b>Controls</b>
<ul style="list-style-type: none"> <li>Children with age between 6 months to 60 months with fever without seizures</li> </ul>	<ul style="list-style-type: none"> <li>Children with central nervous system infections</li> <li>Children with past medical history of seizures of any other etiology</li> <li>Children with CNS malformations, Developmentally challenged</li> <li>Children on micronutrient supplements</li> <li>Children with metabolic disorder, cardiac, kidney disease, gastroenteritis</li> </ul>

**Micronutrient levels**<sup>15</sup>

<b>Micronutrient</b>	<b>Age</b>	<b>Male</b>	<b>Female</b>
Magnesium (mg/dl)	7 days – 2yrs	1.6 – 2.6	1.6 – 2.6
	2 yrs – 14yrs	1.5 – 2.3	1.5 – 2.3

**Statistical Analysis**

The collected data was entered in Microsoft excel. For continuous variables, data were expressed in terms of mean and SD, whereas for categorical variables, data were expressed in

terms of number and percentage. Comparison between case and control groups was performed by using unpaired t-test for parametric data and Mann-Whitney test for non-parametric data. Association between variables was assessed by using Chi-



square test or Fisher's exact test was used for small sample size. A p-value less than 0.05 were considered as significant. Microsoft excel was used to generate tables and graphs. Data analysis was performed by using software SPSS v20.0.

### III. RESULTS

A total of 152 children were enrolled in the study, children with febrile seizures (cases) 76 and children with fever without seizures (controls) 76.

**Table I: - Age distribution of Cases & Controls**

Age (months)	Case N=76	Control N=76
6 - 12	19 (25%)	19 (25%)
13 - 24	31(40.8%)	31(40.8%)
25 - 36	19(25%)	19(25%)
37 - 48	6(7.9%)	6(7.9%)
49 - 60	1(1.3%)	1(1.3%)

**Table II: Gender wise distribution of cases & controls**

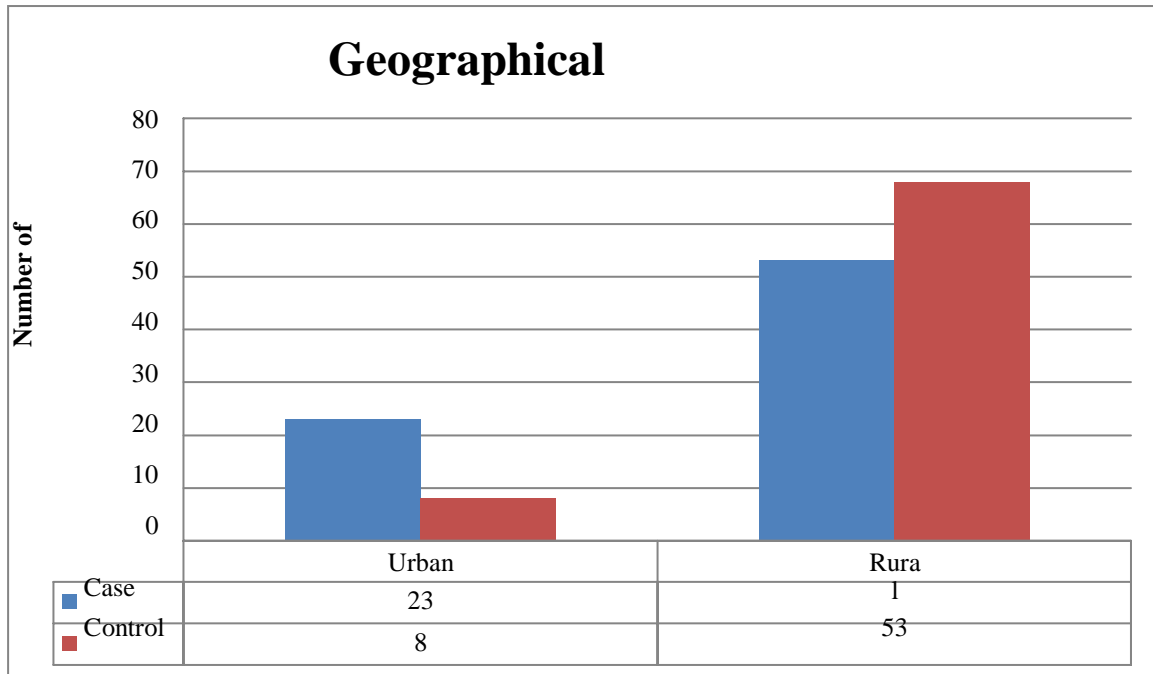
Gender	Case	Control
Male	44 (57.9%)	42 (55.3%)
Female	32(42.10%)	34 (44.7%)
Total	76	76

**Table III: Distribution of children based on geographical area**

Geographical Area (Locality)	Case	Control	Test Statistical Value	P value
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	<b>n=76</b>	<b>n=76</b>		
Urban	23 (30.3%)	8 (10.5%)	152.0	<0.0001
Rural	53 (69.7%)	68 (89.5%)		



**Graph I: Distribution of children based on geographical area**

Table V shows that majority of children of both groups were from rural area (53 cases and 68 controls). Only 23 children among cases and 8 children from

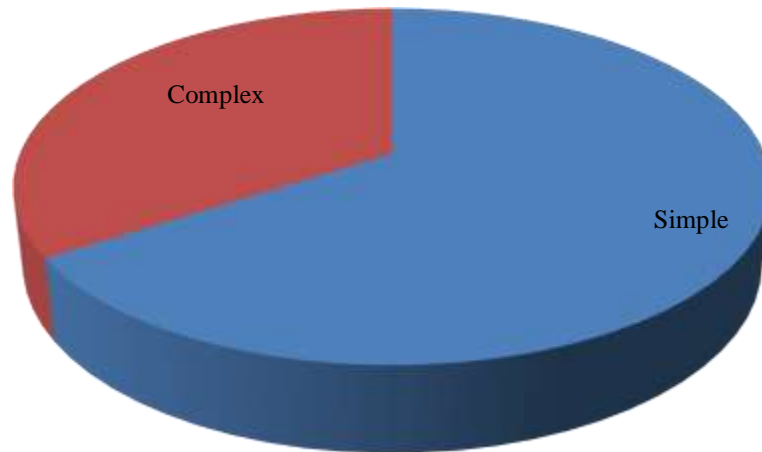
controls belonged to urban area and statistical results showed to be significant ( $p < 0.0001$ ).

**Table IV: Distribution of children based on Type of febrile seizures**

Type of febrile seizures	Frequency	Percentage
Simple	50	65.8 %
Complex	26	34.2 %



## Type of Febrile Seizure



Graph II: Distribution of children based on Type of febrile seizures

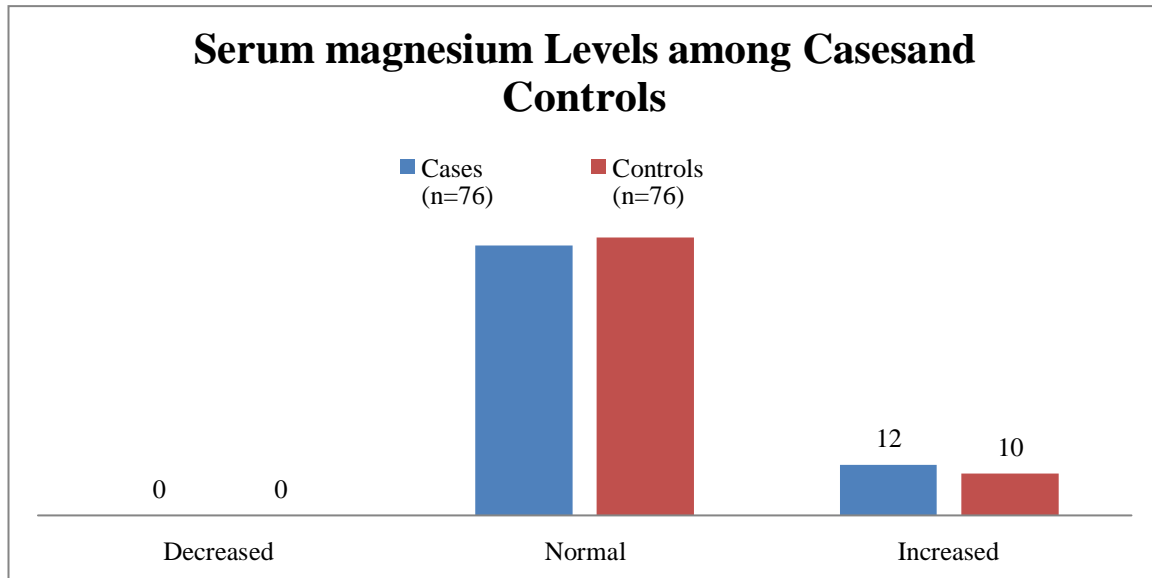
Table IV shows that out of 76 cases, 50 children had simple febrile seizures and 26 children had complex febrile seizures.

In our study, mean values for serum magnesium for cases and controls were  $2.27 \pm 0.31$  and  $2.16 \pm 0.25$  respectively. Mean value was higher in cases and result was statistically significant ( $P=0.02$ ).

### Serum magnesium

Table V- Association of Serum Magnesium among cases and controls

	Cases (n=76)	Controls (n=76)	ChiSquare	P value
Decreased	0	0	0.05	0.41
Normal	64 (84.2%)	66 (86.8%)		
Increased	12 (15.8%)	10 (13.2%)		



**Graph III- Association of Serum Magnesium among cases and controls**

Table V reveals no child had decreased levels of serum magnesium in both the groups, followed by only 12 children in cases and 10 children in controls had increased levels of serum magnesium. Remaining all the children in both the groups

had normal levels of serum magnesium (64 and 66 children among cases and controls respectively) and the results were not statistically significant ( $P=0.41$ ).

**Table VI-Association of Serum Magnesium among cases and controls according to gender distribution**

Gender	Levels	Cases (N=76)	Controls (N=76)	Chi Square	P value
Male	Decreased	0	0	0.04	0.42
	Normal	37 (84.1%)	36 (85.7%)		
	Raised	7 (15.9%)	6 (14.3%)		
Female	Decreased	0	0	0.009	0.46
	Normal	27 (84.4%)	30 (88.2%)		
	Raised	5 (15.6%)	4 (11.8%)		



Table VI shows among male children, normal levels of serum magnesium was seen in 37 cases and 36 controls. 7 children among cases and 6 children among controls had increased levels of serum magnesium. None of the children among males had decreased levels of serum magnesium. Result was not statistically significant (P=0.42)

Among female children, maximum children in both the groups, 27 in cases and 30 in controls had normal levels of serum magnesium. 5 cases and 4 controls had raised serum magnesium. None of the female child had decreased serum magnesium levels and the result was not statistically significant (P=0.46).

**Table VII- Association of Serum Magnesium among cases and controls according to age groups**

Age Group / N	Levels	Cases (N=76)	Controls (N=76)	Chi Square	P value
6-12 months N= 19	Decreased	0	0	0.28	0.29
	Normal	16 (84.2%)	18 (94.7%)		
	Raised	3 (15.8%)	1 (5.3%)		
13-24 months N= 31	Decreased	0	0	0.22	0.32
	Normal	28 (90.3%)	29 (93.5%)		
	Raised	3 (9.7%)	2 (6.5%)		
25- 36 months N=19	Decreased	0	0	0.13	0.36
	Normal	13 (68.4%)	14 (73.7%)		
	Raised	6 (31.6%)	5 (26.3%)		
36-60 months N=7	Decreased	0	0	0.58	0.23
	Normal	7 (100%)	5 (71.4%)		
	Raised	0	2 (28.6%)		



Table VII Shows in age group 13-24 months, 28 children in cases and 29 children in controls had normal serum magnesium levels. Whereas only 3 cases and 2 controls had raised levels of serum magnesium. None in this age group had decreased serum magnesium and result was not statistically significant (P=0.32).

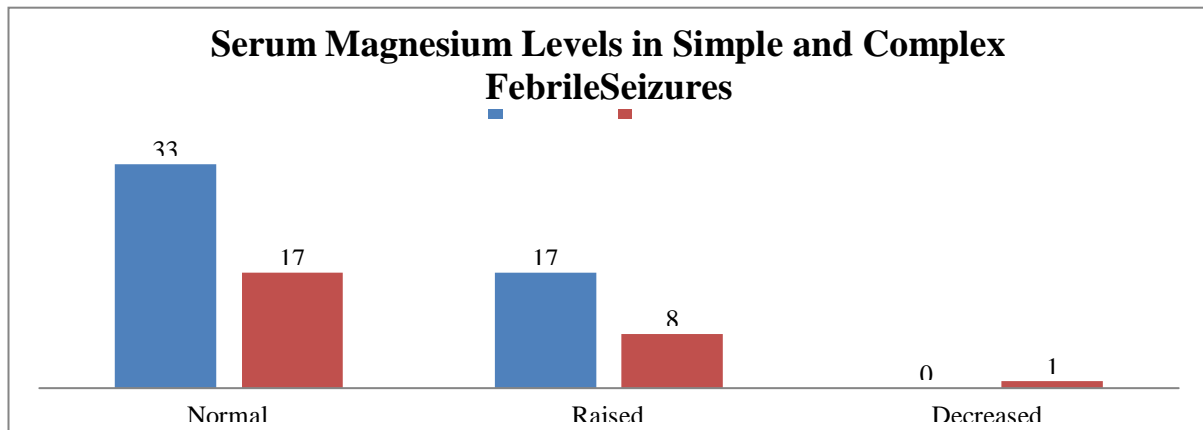
In age group 6-12 months, maximum children had normal levels of serum magnesium (16 cases and 18 controls). 1 control and 3 cases had raised serum magnesium levels. None in this age group had decreased serum magnesium. Result was not statistically significant (P=0.29).

Similarly in age group of 25-36 months, serum magnesium was raised in 6 cases and 5 controls. Majority had normal levels of serum magnesium (13 and 14 in cases and controls respectively). None had decreased serum magnesium level. Result was not statistically significant (P=0.36).

Out of 7 children in the age group of 36-60 months, none had decreased serum magnesium. All 7 cases and 5 controls had normal serum magnesium. 2 controls had raised serum magnesium. Result was not statistically significant (P=0.23).

**Table VIII: Association of Serum magnesium levels with Simple and Complex febrile seizures**

Serum Magnesium	Type Of Febrile Seizures (%)		Chi-Square Value	P-Value
	Simple	Complex		
Normal	40 (80%)	24 (92.3%)	1.13	0.29
Raised	10 (20%)	2 (7.7%)		
Decreased	0	0		



**Graph IV: Association of Serum magnesium levels in Simple And Complex febrile seizures**

Table VIII shows that the serum magnesium levels were normal in 40 children with simple febrile seizure and 24 Children with complex febrile seizures. None had decreased serum magnesium

level. It was raised in 10 children with simple febrile seizures and 2 children with complex febrile seizures and the results are not statistically significant (p=0.29).

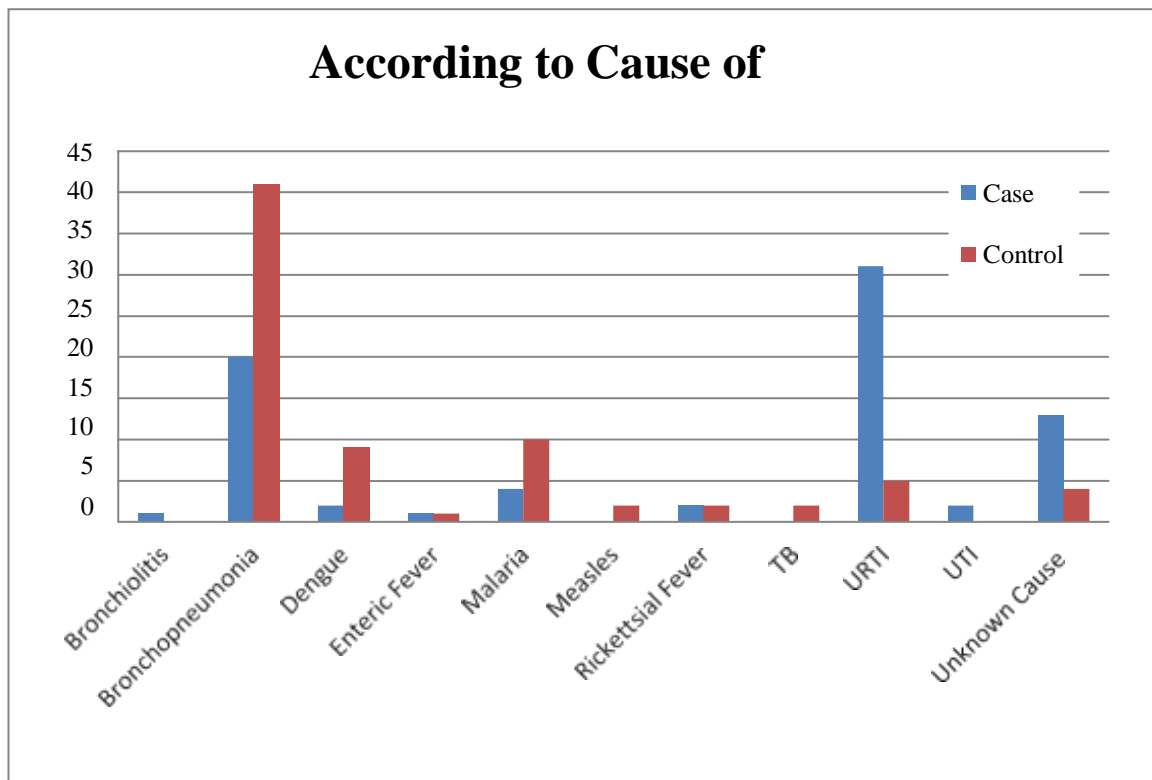
**Table IX: Distribution according to Cause of Fever among cases and controls**

Causes of fever	Cases	Controls
Bronchiolitis	1 (1.3%)	0
Bronchopneumonia	20 (26.3%)	41 (54%)





Dengue	2 (2.6%)	9 (11.8%)
Enteric Fever	1 (1.3%)	1 (1.3%)
Malaria	4 (5.3%)	10 (13.2%)
Measles	0	2 (2.6%)
Rickettsial Fever	2 (2.6%)	2 (2.6%)
TB	0	2 (2.6%)
URTI	31 (40.8%)	5 (6.6%)
UTI	2 (2.6%)	0
Unknown Cause	13 (17.1%)	4 (5.3%)



Graph V: Distribution according to Cause of Fever among cases and controls

### Serum Magnesium

#### Comparison of Mean Serum Magnesium Levels

Table X Comparison of Mean Serum Magnesium Levels

Study	Cases	Controls	P value
Our study	2.27 ± 0.31	2.16 ± 0.25	0.02
UshaKiran et al <sup>16</sup>	1.85 ± 0.26	1.79 ± 0.22	0.1978



SepidehAmouian et al <sup>17</sup>	2.38 ± 0.57	2.40 ± 0.58	Not significant
Namkin K et al <sup>18</sup>	1.9 ± 0.32	2.27 ± 0.38	<0.001
Talebian et al <sup>19</sup>	2.21	2.39	0.003

In our study, mean serum magnesium levels were  $2.27 \pm 0.31$  in cases and  $2.16 \pm 0.25$  in control, which was **statistically significant (p = 0.02)**. Similarly UshaKiran et al<sup>16</sup> observed the serum magnesium levels were higher ( $1.85 \pm 0.26$ ) among cases than ( $1.79 \pm 0.22$ ) among controls and the result was not significant (P=0.197). SepidehAmouian et al<sup>17</sup> in their case control study found that the serum magnesium levels were lower in cases ( $2.38 \pm 0.57$ ) than controls ( $2.40 \pm 0.58$ ) but statistically not significant. In the study conducted by Namkin K et al,<sup>18</sup> mean serum magnesium levels of  $1.9 \pm 0.32$  in cases and  $2.27 \pm 0.38$  in controls, the result was significant (p<0.001). Talebian et al<sup>19</sup> observed the mean serum magnesium levels of 2.21 among cases and 2.39 among controls and the result was statistically significant (P=0.003). **Above all the studies, including our study showed that mean values of serum magnesium levels in both cases and controls were within normal limits.**

#### Serum Magnesium and Type of Febrile Seizure

In our study, the serum magnesium levels was normal in 80% children with simple febrile seizures and 92.3% children with complex febrile seizures, and raised in 20% children with simple febrile seizure and 7.7% children among complex febrile seizures and the result was not statistically significant (P = 0.29). Similarly in study done by Talebian et al,<sup>19</sup> there was no significant difference in serum magnesium levels between simple and complex febrile seizures (p=0.961).

#### Serum Magnesium among Cases and Controls According To Gender Distribution

In present study among males, maximum children in cases (84.1%) and controls (85.7%) had normal serum magnesium levels. It was increased in 14.3% of controls and 15.9% of cases. Similar findings were observed among females, with normal values of serum magnesium in 84.4% cases and 88.2% controls. It was raised in 11.8% of controls and 15.6% of cases. None among males and females had decreased serum magnesium. The result was statistically not significant for males and females (P value 0.42 and 0.46 respectively).

We did not found data in other studies comparing serum magnesium with febrile seizures according to gender distribution

#### IV. SUMMARY AND CONCLUSION

- The mean age of presentation of children with febrile seizures in our study group was  $23.5 \pm$  months. Majority of children belonged to age group 13 - 24 months.
- Male predominance was seen among children with febrile seizures, with male to female ratio of 1.37:1.
- In our study, among cases, simple febrile seizures were more common (65.8%) than complex febrile seizures (34.2%).
- Mean values for serum magnesium levels for cases and controls were  $2.27 \pm 0.31$  and  $2.16 \pm 0.25$  respectively and result was statistically significant. (p=0.02) Although mean values were higher in cases than controls, both were in normal range. It indicates that serum magnesium may not have a significant role in etiopathogenesis of febrile seizures.
- It was concluded that there was no significant association of serum magnesium level in children with febrile seizure in relation to age groups and gender.
- In our study, majority of children with febrile seizures and controls were from rural area with significant association.
- Our study also revealed that there is no significant difference in serum magnesium levels between simple and complex febrile seizures.
- Our study revealed that respiratory infections were predominant cause of fever among cases as well as controls. Upper respiratory tract infection was the predominant cause of fever among children with febrile seizures.
- Thus in our study, the mean serum levels of Magnesium were within normal limits in cases of febrile seizures as well as controls. Hence it may be concluded that the serum levels of magnesium were not related to the occurrence of febrile seizures.



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