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Research Article

Comparison of Serum Zinc Level in Patients with Simple Febrile Seizure versus Acute Febrile Illness

Vidyasagar V[1], Venugopal BL[2], Darshan MS[3]
[1]Assistant Professor, [2]Assistant Professor, Department of Paediatrics, Kannur Medical College, Anjarakandy, Kannur, Kerala, India
[3]Assistant Professor, Department Of Anaesthesiology, CIMS, Chamarajanagar, Karnataka, India

***Corresponding author**
Darshan MS
Email: vidyasagar103@gmail.com

Abstract: Febrile seizure is a common illness in children in the age group of 6 months to 5 years. The role of microelements like zinc has been studied in febrile seizures previously, but fever is known to reduce serum zinc levels. The present study aims to compare serum zinc in children with simple febrile seizures and acute febrile illness. A hospital based comparative study, consisting of infants and children aged between 6 months to 5 years, 80 children each in two groups i.e. group A and group B shall be included for the study. Group-A: children with simple febrile seizures aged between 6 months to 5 years. Group –B: children with acute febrile illness aged between 6 months to 5 years. Serum Zinc estimation done in both groups by colorimetric method and compared using various statistical tests. Mean serum Zinc level was lower in group A (59.93µgm/dl) compared to group B (69.99µgm/dl), and was a statistically significant (p=0.001). Serum zinc level was lower in children with simple febrile seizures as compared to children with acute febrile illness.
Keywords: serum zinc, acute febrile seizure, acute febrile illness, GABA, glutamate, hypozincemia.

INTRODUCTION

The study intends to investigate the role of zinc in the causation of febrile seizures. Febrile seizures occur in 2–4 % of all children [1, 2]. Various studies have shown trace elements like Magnesium [3, 4], Sodium [5], Selenium [6], Iron [7, 8] and Zinc [3, 4, 9, 10, 11] may have a role in causation of febrile seizures.

The role of Zinc in the causation of febrile seizures has been described based on two important mechanisms. Firstly, Zinc deficiency lowers serum and CSF concentration of γ-amino butyric acid (GABA) secondly, hypozincemia activates the NMDA receptor, one of the glutamate family receptors, which may play an important role in the induction of epileptic electrical discharges [12], Gamma-amino butyric acid (GABA), a major inhibitory neurotransmitter, is produced by decarboxylation of L-glutamate. Glutamic acid decarboxylase is the rate limiting enzyme of GABA synthesis and requires pyridoxal phosphate or vitamin B6 for its activity. Zinc stimulates the activity of pyridoxal kinas, the enzyme that forms pyridoxal phosphate from pyridoxal, and thereby modulates the activity of glutamic acid decarboxylase and the synthesis of GABA[8]. During fever, there is a acute phase response is mediated by cytokines such as interleukin 1 (IL-1) and tumour necrosis factor α, which are secreted primarily by monocytes and activated macrophages in response to infection or injury [13], this may cause a decreased serum zinc level.

METHODOLOGY

Source of Data

The proposed study was a hospital based comparative study, done at a tertiary care centre in South India consisting of infants and children aged between 6 months to 5 years.
80 children each in two groups i.e. Group A and Group B shall be included for the study.
Group-A: children with simple febrile seizures aged between 6 months to 5 years
Group –B: children with acute febrile illness aged between 6 months to 5 years

Sampling Method: Purposive sampling technique.

Inclusion Criteria: Children with simple febrile seizure and children with acute febrile illness without seizures who were aged between 6 months to 5 years.

Exclusion Criteria:

Children with Diarrhoea, Pneumonia, Protein Energy Malnutrition, Developmental delay and Children on zinc therapy. A total of 160 infants and

children aged between 6 months to 5 years admitted in our hospital during the study period fulfilling the inclusion criteria were included. 80 children in Group A with simple febrile seizure and 80 children in Group B comprised of children with acute febrile illness without seizure.

A written informed consent was obtained from parents/guardians of all the children after fully explaining the study procedure. Socio-demographic data, seizure details, nature of febrile illness, family history of epilepsy/ febrile seizures, temperature at admission, nutritional status and vital signs namely heart rate, respiratory rate and blood pressure were measured. The axillary temperature was recorded in all children with mercury thermometer placed in axilla for three minutes, followed by general examination and systemic examination in detail. The findings were recorded in a predesigned Performa.

Under aseptic precaution, 2ml of blood from venipuncture using 22 gauge sterile needle was collected in morning, non fasting state within 24 hours of contact of patient in both the groups. The sample was centrifuged for 3-4 minutes at 3000-4000rpm; serum thus obtained is collected and preserved at 2-8°C in sterile deionised plain vials. Serum sample collected will be deprotinised with 5-Br-PAPS, 2((5-BROMO-2-PYRIDYLAZO)-5-(N-PROPYL-NSULFOPROPYL-AMINO)-PHENOL reagent. The complex formed was measured at a wave length of 560nm. Intensity of colour formed is directly proportional to the amount of zinc present in the sample. In the present study serum zinc level less than 65 micro gram/dl was taken as cut off for zinc deficiency [14]. The two groups included in the study were compared with respect to serum zinc level and demographic characteristics.

STATISTICAL METHODS APPLIED

Descriptive statistics

The Descriptive procedure displays univariate summary statistics for several variables in a single table and calculates standardized values.

Contingency table analysis

The Cross tabs procedure forms two-way and multiway tables and provides a variety of tests and measures of association for two-way tables.

Independent-Samples T Test

The Independent-Samples T Test procedure compares means for two groups of cases.

2-way ANOVA (GLM-General Linear Model)

The GLM Univariate procedure provides analysis of variance for one dependent variable by one or more factors and/or variables. The factor variables divide the population into groups. All the statistical calculations were done through SPSS 16.0 (2007) for windows.

RESULTS

Table 1 represents the distribution of population of both the groups at different age groups. The age distribution was similar in both the groups and majority of cases were of less than two years in both the groups.

Table 2 represents the mean age between GROUP A and GROUP B. Results showed that there was no statistically significant difference in mean age between GROUP A and GROUP B (P=0.168).

Table 3 represents sex distribution between group A and group B. Results showed that there was no statistically significant difference in the sex distribution between GROUP A and GROUP B (P=0.874).

Table 4 shows 19 out of 80 had a past history of febrile seizure in group A. Among them 12 had history of previous episode and 6 had a history of 2 previous episodes 1 patient had a history of previous 3 episodes.

Table 5 represents the children with family history of febrile seizure. 17(21.2%) out of 80 in group A had a family history of febrile seizure. Among them 10 had history febrile seizure in a sibling, 5 had similar history in a parent and 2 had in a similar history in second degree relative.

Table 6 represents the distribution of Socio Economic Status in Group A and Group B. 49% in Group A 62.5% in Group B belonged to class IV socioeconomic status. Classification of socioeconomic status was done as per modified Kuppu swamy classification [15]. There was no statistically significant difference in the socio economic status among Group A and Group B (p=0.348).

Table 7 represents the comparison of height between GROUP A and GROUP B. There was no statistically significant difference in variation of height between the two groups (p=0.296).

Table 8 represents the comparison of weight between GROUP A and GROUP B. There was no statistically significant difference in variation of weight between the two groups (p=0.61).

Table 9 represents the comparison of Head Circumference between GROUP A and GROUP B. There was no statistically significant difference in Head Circumference between the two groups (p=0.61)

Table 10 represents the mean temperature at admission measured in the axilla between the two groups. In the mean temperature was slightly higher in Group A compared to Group B. There was no statistically significant difference (P=0.282).

Table 11 represents the mean serum Zinc level in the two groups. It was lower in Group A compared to Group B and was statistically significant (P=0.000).

Serum Zinc level of 65 µgm/dl was considered as cut off for Zinc deficiency[14] .Table 12 shows 60% of Group A and 33.8% in Group B had serum Zinc level < 65 µgm/dl. There was a statistically significant difference between the two groups (P = 0.001).

Table 13 represents the mean serum Zinc level in the different age groups in group A and group B. There was no statistically significant difference (p=0.057) in mean serum Zinc level in relation to different age groups.

Table 14 shows the comparison of mean serum Zinc level in different socioeconomic status in between group A and group B. Majority of the children belonged class III and class IV socioeconomic status in both the groups. There was a statistically significant difference in mean serum Zinc level in class III (p=0.021) and class IV socioeconomic status (p=0.010) in between Group A and Group B.

Table 15 shows there was a lower mean serum Zinc level in group A in both males and females separately , however there was no statistically significant difference(p=0.565) in mean serum Zinc level in relation to sex.

Table 16 represents the different diagnosis in both the groups. Viral fever constituted of 51 cases (63.8%) in group A followed by AURI (25%).Similarly in group B, viral fever constituted 40 cases (50%) in, followed by AURI comprising of 41.3% cases.

Table 1: Age distribution

AGE GROUPS (months)	GROUP A		GROUP B	
	N	%	N	%
6-12	29	36.3	16	28.1
13-24	28	35.0	34	38.8
25-36	12	15	24	22.5
37-48	6	7.5	3	5.6
49-60	5	5	3	5
TOTAL	80	100	80	100

GROUP A= Simple febrile seizure, GROUP B= Acute febrile illness without seizures.

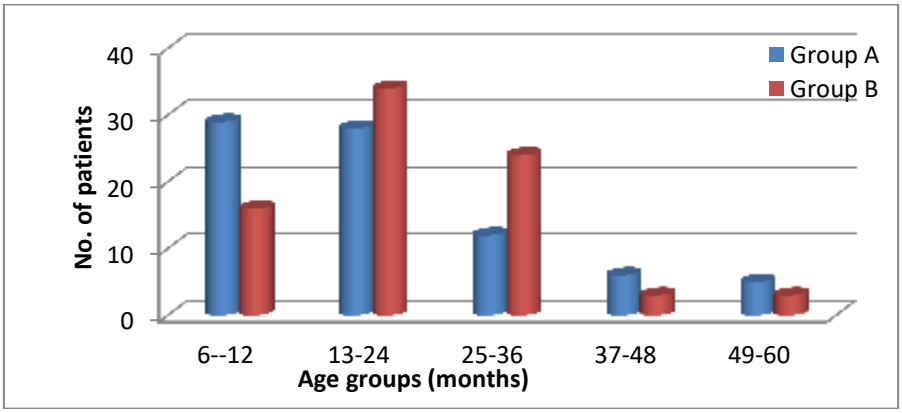

Fig 1: Age distribution

Table 2: Mean age between GROUP A and GROUP B

	Groups	N	Mean	Std. Deviation
Age (months)	GROUP A	80	22.72	14.90
	GROUP B	80	25.67	11.90

t=-1.3, p=0.168.

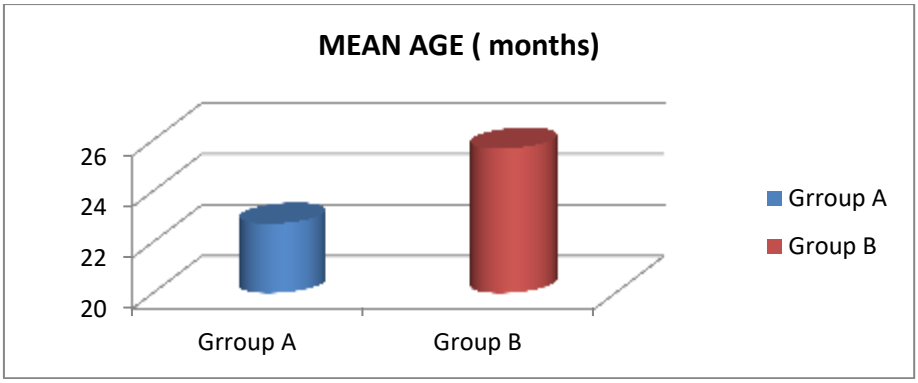

Fig 2: Mean age in group A and group B.
GROUP A= Simple febrile seizure, GROUP B= Acute febrile illness

Table 3: Sex distribution

Gender	GROUP A		GROUP B	
	N	%	N	%
Male	45	56.3	44	55
Female	35	43.8	36	45

Contingency coefficient=0.013, p=0.874.

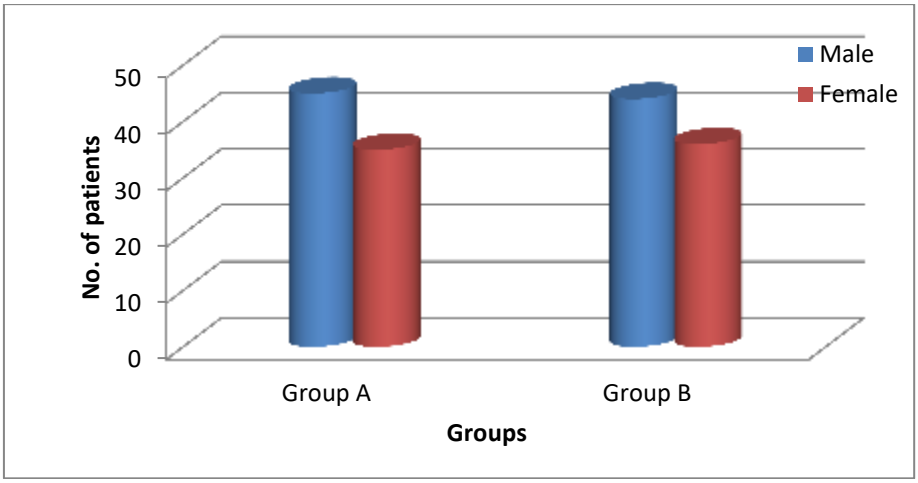

Fig 3: Sex distribution
GROUP A= Simple febrile seizure, GROUP B= Acute febrile illness

Table 4: Past history febrile seizure in group A

GROUP	Group A	
	N	%
Present	19	23.8
Absent	61	77.2

Table 5: Family history of febrile seizure in Group A.

GROUP	Group A	
Family history	N	%
Present	17	21.2
Absent	63	79.8

Table 6: Distribution of Socio-Economic Status (as per modified Kuppu swamy classification)

SOCIO-ECONOMIC STATUS	GROUP A		GROUP B	
	N	%	N	%
CLASS I	2	2.5	0	0
CLASS II	8	10	7	8.8
CLASS III	19	23.8	23	42
CLASS IV	49	49	50	62.5
CLASS V	2	2.5	0	0
TOTAL	80	100	80	100

Contingency coefficient=0.165, p=0.348.

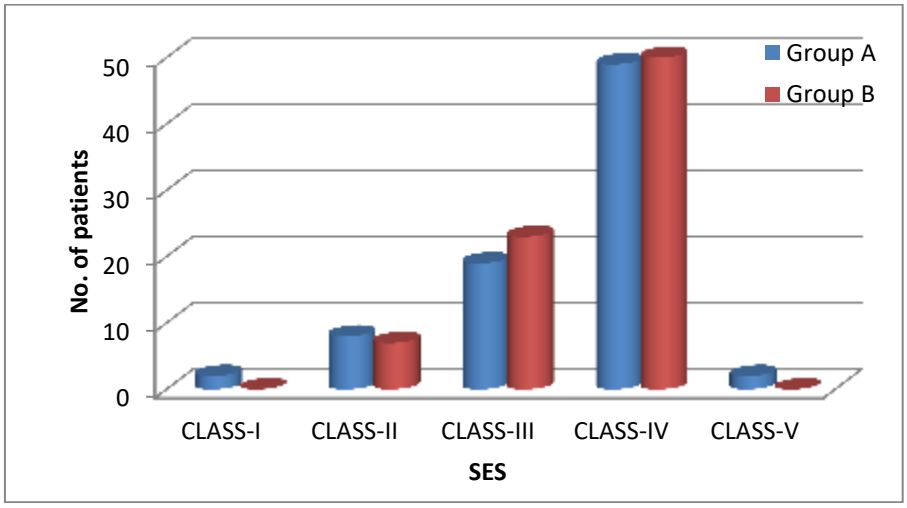

Fig 6: Distribution according to socioeconomic status

Table 7: Comparison of Height between GROUP A and GROUP B

VARIABLES	Mean ± Std. Deviation		Mean difference	t-value	p-value
	GROUP A	GROUP B			
Height (cm)	82.43±12.2	84.24±9.4	-1.81	-1.048	0.296

Table 8: Comparison of weight between GROUP A and GROUP B

VARIABLES	Mean ± Std. Deviation		Mean difference	t-value	p-value
	GROUP A	GROUP B			
Weight(kg)	12.17±6.73	12.6±3.11	-0.42	-0.51	0.61

Table 9: Comparison of Head Circumference between GROUP A and GROUP B

VARIABLES	Mean ± Std. Deviation		Mean difference	t-value	p-value
	GROUP A	GROUP B			
Head circumference(cm)	46.11±2.98	46.7±1.90	-0.58	-1.47	0.141

Table 10: Comparison of mean temperature between the two groups

VARIABLE	Mean ± Std. Deviation		Mean difference	t-value	p-value
	GROUP A	GROUP B			
Temperature (° C)	38.66±0.39	38.60±0.29	0.06	1.079	0.282

Table 11: Comparison of mean serum Zinc level between GROUP A and GROUP B

Variables	Serum Zinc level (µgm/dl)	Mean difference	t-value	p-value
GROUP A	59.53±14.87	-10.45	-4.06	0.000
GROUP B	69.9±17.5			

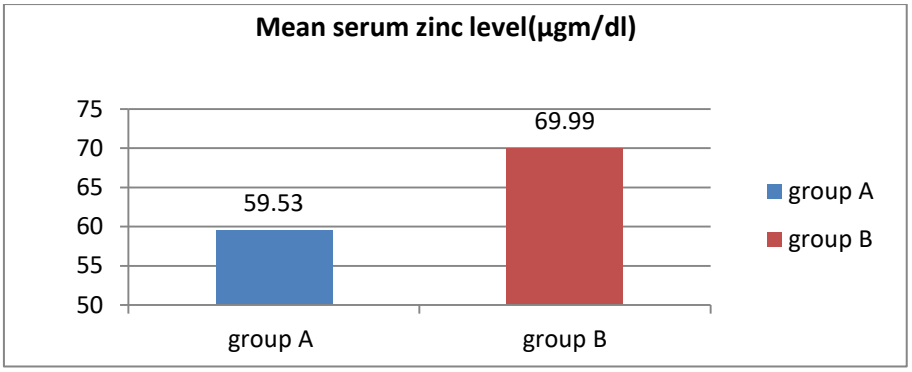

Fig 11: Comparison of serum Zinc levels between GROUP A and GROUP B

Table 12: Comparison of Zinc deficiency among Group A and Group B

	GROUP A		GROUP B		TOTAL	
	N	%	N	%		
Zinc level <65µgm/dl	48	60	27	33.8	75	46.3
Zinc level >65µgm/dl	32	40	53	66.3	85	54.2

Contingency coefficient=0.254,P=0.001.

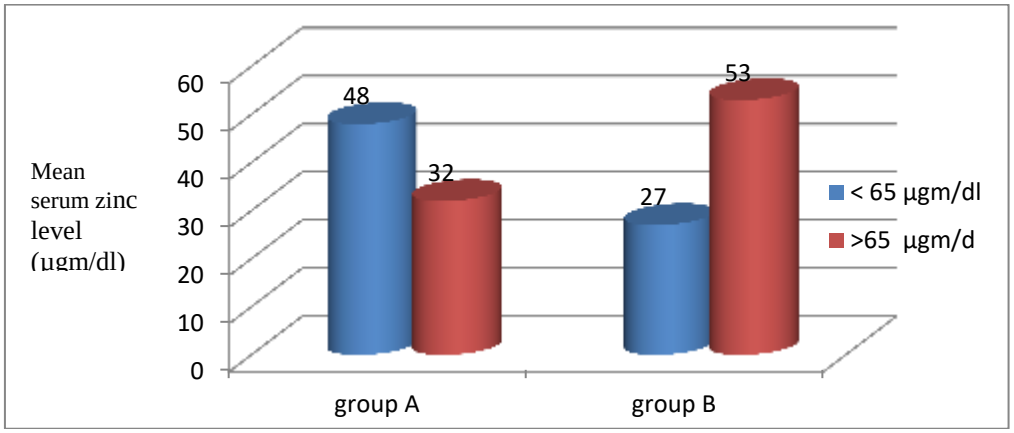

Fig 12: Comparison of Zinc deficiency among group A and group B.

Table 13: comparison of mean serum Zinc level (µgm/dl) in different age groups between Group A and Group B.

Age group(months)	Mean serum Zinc level(µgm/dl)	
	Group A	Group B
6—12	58.0172	65.8562
13-24	60.0643	68.0294
25-36	52.6167	73.2542
37-48	73.3	86.8
49-60	65.46	71.3667

p=0.057

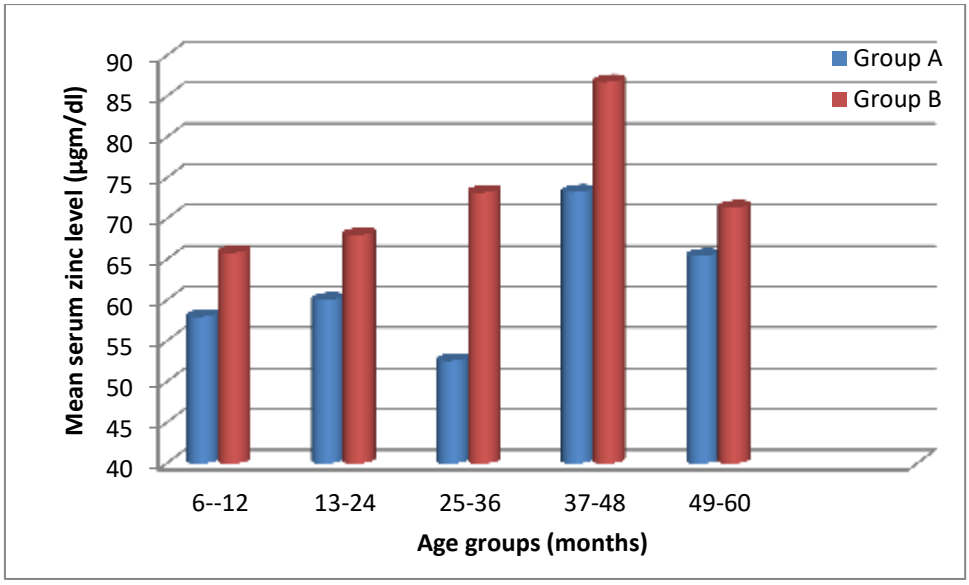

Fig 13: Mean serum Zinc level (µgm/dl) in different age groups between Group A and Group B

Table 14: Comparison of mean serum Zinc level (µgm/dl) in patients in different Socio economic status (as per modified Kuppu swamy classification 15) between Group A and Group B.

	Mean Serum Zinc level(µgm/dl)		P value
SOCIOECONOMIC STATUS	GROUP A	GROUP B	
CLASS-I	50.35	0	
CLASS-II	58.2625	73.4143	0.103
CLASS-III	58.1421	70.2217	0.021
CLASS-IV	60.8245	69.406	0.010
CLASS-V	55.45	0	

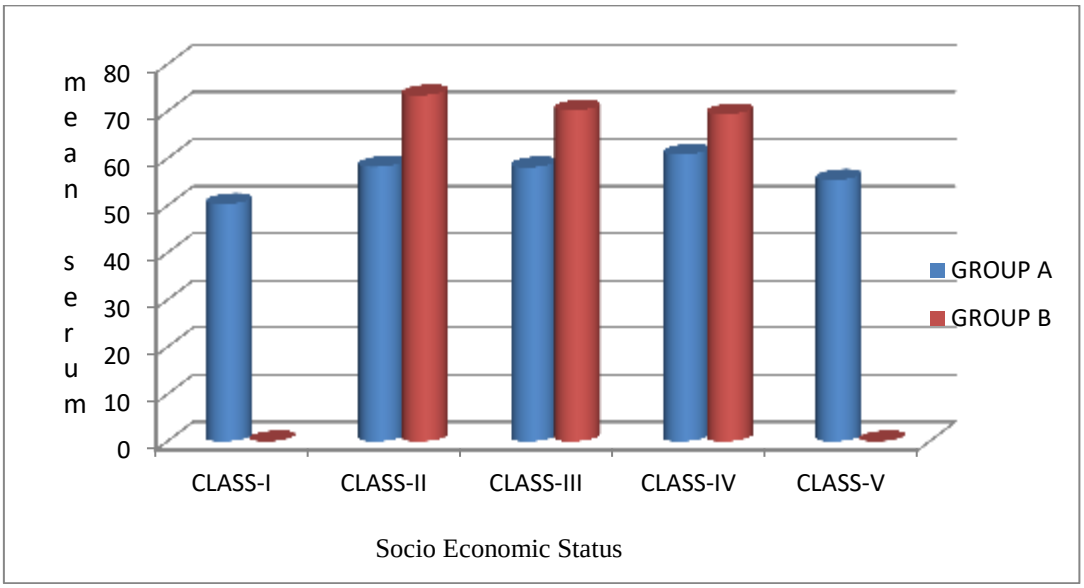

Fig 14: Comparison of mean serum Zinc level (µgm/dl) in patients in different socioeconomic status (as per Modified Kuppu swamy classification[15]) in between group A and group B.

Table 15: Comparison of mean serum Zinc level among children based on gender in Group A and Group B

SEX	GROUP A		GROUP B	
	N	Mean serum Zinc(µgm/dl)	N	Mean serum Zinc(µgm/dl)
Male	45	61.08	44	69.74
Female	35	57.53	36	70.29

, p=0.565

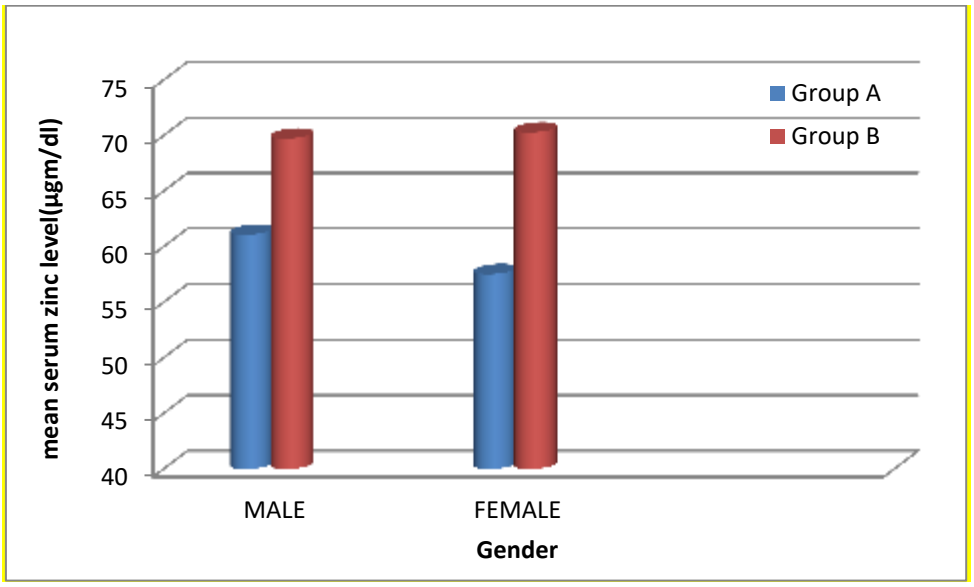

Fig 15: Comparison of mean serum Zinc level among children in different sex in between Group A and Group B

Table 16: Distribution of diagnosis in GROUP A and GROUP B

Diagnosis	GROUP A		GROUP B	
	N	%	n	%
AURI	20	25	33	41.3
VF	51	63.8	40	50
UTI	4	5	3	3.8
ASOM	5	4	4	5
Total	80	100	80	100

(AURI-acute upper respiratory tract infection, VF-viral fever, UTI-urinary tract infection, ASOM- Acute Suppurative Otitis Media)

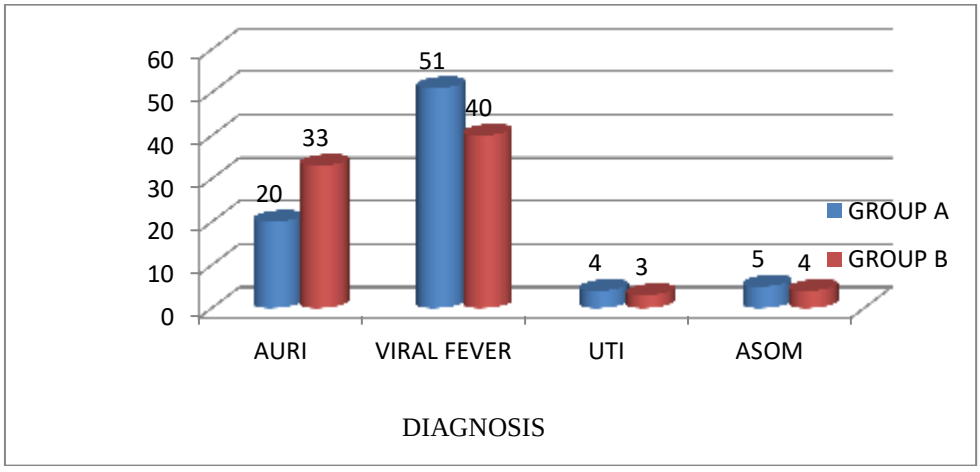

Fig 16: Distribution of diagnosis in Group A and Group B.

AURI=Acute Upper Respiratory Infection, UTI=Urinary Tract Infection, ASOM=Acute Suppurative Otitis Media.

DISCUSSION

Mean age in our study did not show statistically significant difference (p=0.168) in between the two group. Studies done by Ganesh R *et al.;* [11], Heydarian *et al*.; [3], Amiri M *et al*.; [16] and Margaretha *et al*.; [10] showed no statistically significant difference in the two groups. There was no statistically significant difference in the mean serum Zinc level in relation to age, (p=0.057) similar findings were reported by Ganesh R *et al.;* [11], Talebian *et al*.; [4] Kafadar *et al*.; [17]. There was no statistically significant difference in the mean serum Zinc level in relation to sex(p=0.565), similar findings were reported by Ganesh R *et al*.; [11], Amiri M *et al*.; [16] and Talebian A *et al*.; [14] who reported no difference in serum Zinc level in relation to sex. In the present study, mean temperature was higher in children with simple febrile seizure compared to children with acute febrile illness. However, no statistically significant difference was found in the mean temperature between the two groups in our study (p=0.282). In the present study 19 (23.5%) children had a past history of febrile seizure. Kafadar I *et al*.; [17] in their study conducted in Turkey, reported past history of febrile seizures as 33.4%. The higher incidence may be due to the difference in geography and race. In the present study 17 (21.2%) of children had family history of febrile seizure, similar results were found in a study conducted in Kerala by Kumari PL *et al*.; [18] In both groups, group A (46%) and group B (62.5%) maximum distribution was in class IV socio economic status as per modified Kuppu swamy classification. There was no statistically significant difference in the socioeconomic class distribution between the two groups (p=0.348). In the present study mean serum Zinc level was lower in children with simple febrile seizures than children with acute febrile illness without seizures.

There was a statistically significant difference in mean serum Zinc level in between children with simple febrile seizures and acute febrile illness without seizures (p=0.000). In the present study there is no decrease in mean serum Zinc level compared to the cut off value less than 65 µgm/dl as suggested by IZiNCG [14] in children with acute febrile illness. Similar findings were noted by Ganesh R *et al.;* [11]. Hence serum Zinc was normal in children with acute febrile illness without seizures. Burhangnoglu M *et al*.; [9] found lower mean serum Zinc level and also CSF Zinc level in children with febrile seizure than the other groups. In the present study CSF Zinc was not measured. Mahyar A *et al*.; [6], considered febrile seizure group as cases and healthy children as controls found that there was decrease in serum Zinc level in cases compared to control group, however in the present study Group-B consisted of acute febrile illness without seizures.

Amiri M *et al*.; [15] compared Selenium, Zinc level and Copper level in serum between the two groups reported that serum Zinc and Selenium were lower in febrile Seizure group compared to control group no significant difference in serum copper level. Margaretha *et al*.; [10] found that there is a correlation between serum Zinc level and febrile seizure and lesser the serum Zinc level longer the duration of seizure. Modarresi MR *et al*.; [19] found that serum Zinc level was lower in children with febrile seizure than the other two control groups, which included febrile children and healthy children. In the present study serum Zinc level was less than cut-off value of 65µgm/dl in 60% children in simple febrile seizure and 33.8% in children with acute febrile illness, there was a statistically significant difference between the two groups (p=0.001), similar findings were reported by Mahyar A *et al*.; [6] but the cut-off for serum Zinc was considered as less than 70µgm/dl. The cut-off values in the present study are based on the recommendations for indicators of population Zinc status of WHO / UNICEF / IAEA / IZINCG consensus.

Zinc is an essential micronutrient required for the normal function and development of the central nervous system. Zinc has a role in modulation of neurotransmission by inhibitory effect on the Glutamatergic NMDA receptor, and by acting as a cofactor to the rate limiting enzyme in GABA synthesis. Thus Zinc deficiency can lead to the excitation inhibition imbalance leading to a febrile seizure. Hence Zinc deficiency may play a role in mechanism of febrile seizures.

CONCLUSION

Serum zinc level was lower in children with simple febrile seizures as compared to children with acute febrile illness which was found to be statistically significant.

LIMITATIONS

Zinc estimation in the present study was done by colorimetric method. Atomic absorption spectrometry (AAS) is a more accurate method to measure serum zinc level. Though AAS was not done, there is a good correlation between AAS and colorimetric method20 which is used in the present study. Blinding in our study was not possible.

REFERENCES

1. American Academy of Paediatrics, American Academy of Pediatrics: Provisional Committee on Quality Improvement. Practice parameter: The neuro diagnostic evaluation of the child with a simple febrile seizure. Paediatrics 1996; 97:769.
2. Berg AT; The epidemiology of seizures and epilepsy in children. In: Shinnar S., Amir N., Branski D., ed. Childhood seizures, Basel, Switzerland: S Karger; 1995.
3. Heydarian F, Ashrafzadeh F, Ghasemian A; Serum Zinc level in patients with simple febrile seizure. Iran J Child Neurology, 2010; 4(2): 41-44.

4. Talebian A, Vakili Z, Talar SA, Kazemi M, Mousavi GA; Assessment of the relation between serum zinc and magnesium levels in children with febrile convulsion. Iranian journal of pathology 2009; 4:157-160.
5. Thoman J, Duffner P, Shucard J; Do serum sodium levels predict recurrent febrile seizures within 24 hours? Pediatr Neurol, 2004; 31(5): 342-4.
6. Mahyar A, Ayazi P, Fallahi M, Javadi A; Correlation between serum selenium level and febrile seizures. Pediatr Neurol, 2010; 43(5): 331-4.
7. Daoud AS, Batieha A, Abu-Ekteish F, Gharaibeh N, Ajlouni S, Hijazi S; Iron status: a possible risk factor for the first febrile seizure. Epilepsia. 2002; 43(7): 740-3.
8. Ebadi M, Wilt S, Ramaley R; The role of zinc and zinc-binding proteins in regulation of glutamic acid decarboxylase in brain. Chemical and biological aspects of vitamin B_6.Catalysis. New York: Alan R Liss, 1984 (part A): 255-75.
9. Barhanoglu M, Tutuncuoglu S, coker C, Tekgul H, ozgurT; Hypozincemia in febrile convulsion. Euro J pediatr, 1996; 155(6): 498-5010.
10. .garetha L, Masloman N; Correlation between serum zinc level and simple febrile seizure in children. Pediatr in dones, 2010; 50(6): 326-330.
11. Ganesh R, Janakiraman L; Serum zinc levels in children with simple febrile seizure. Clin Pediatr (Phila), 2008; 47: 164-6.
12. Izumi Y, Ishii K, Akiba K, Hayashi T; Hypozincemia during fever may trigger febrile convulsion. Med Hypotheses. 1990 May; 32(1):77-80.
13. Cousins RJ, Leinart AS; Tissue-specific regulation of Zinc metabolism and metallo thionein genes by interleukin 1. FASEB 1988; 2: 2884–90.
14. Executive summary. Recommendations for indicators of population Zinc status. Report of WHO / UNICEF / IAEA / IZincG Interagency Meeting on Zinc Status Indicators. Food Nutr Bull, 2007; 28: S399-S400.
15. Kumar N, Shekhar C, Kumar P, Kundu AS; Kuppuswamy's Socioeconomic Status Scale-Updating for 2007Indian Journal of Pediatrics, 2007; 74: 77-78.
16. Amiri M, Farzin L, Moassesi ME, Sajadi F; Serum Trace Element Levels in Febrile Convulsion, Biol Tr Elems , 2010; 135 (1): 38-44.
17. Kafadar I, Akıncı AB, Pekün F, Ada E; The Role of Serum Zinc Level in Febrile Convulsion Etiology. J Pediatr Inf, 2012; 6: 90-3.
18. Kumari PL, MKC Nair, SM Nair; Iron Deficiency as a Risk Factor for Simple Febrile Seizures– A Case Control Study, Indian Paediatrics, 2011.
19. Modarresi MR, Shahkarami SMA, Yaghini O, Shahbi J, Mosaiiebi D, Mahmoodian T; The relationship between Zinc deficiency and Febrile Convulsion in Isfahan, Iran. Iranian Journal of Child Ne urology 2011; 5(2): 27-31.
20. Beckett JM, Hartley TF, Ball MJ; Evaluation of the Randox colorimetric serum copper and zinc assays against atomic absorption spectroscopy. Ann 2009; 46(Pt 4): 322-6