

A Study on Prevalence and Association of Anaemia and Hyponatremia in Simple Febrile Seizures in Children

GN BHARAT KUMAR, BS SRINIVASA, SK MANUPRAKASH, ARA SYEDA SALTANAT, DG PRASANNA KUMAR, HR SUMA

ABSTRACT

Introduction: Febrile seizures are common type of seizures in children which occurs between 6 months to 60 months of life, usually single episode within 24 hours of onset of fever. It lasts for less than 15 minutes with a brief period of post-ictal drowsiness without any neuroinfection.

Aim: To find the prevalence of anaemia and hyponatremia in simple febrile seizures and also the association of anaemia and hyponatremia in children with simple febrile seizures.

Materials and Methods: The cross-sectional study was conducted from November 2013 to November 2015. The sample constituted 120 children belonging to the age group of 6 months to 5 years presenting with simple febrile seizures in the Pediatrics department of Sri Chamarajendra Hospital(SCH), Hassan Institute of Medical Sciences, Hassan. The following data were collected-duration of fever, time of onset of seizures, type of seizures, duration of seizures, medical and family history of seizures in first degree relatives, consanguinity and history on trigger

for febrile episode. Anaemia was evaluated by complete blood count analysis with manual peripheral smear examination while hyponatremia was assessed by doing electrolyte analysis using Transasia automated analyser by ion selective electrode method. The data was analysed by using chi-square test.

Results: In total 120 children with simple febrile seizures were studied and majority of them belonged to 6months to 2years of age (61.6%).The study showed a significant association between anaemia and febrile seizures ($p<0.02$), a significant association between Hyponatremia and febrile seizures ($p<0.05$) and a significant association between anaemia and hyponatremia in simple febrile seizures ($p<0.001$). Prevalence of anaemia was 50% where as hyponatremia was 35.8%; as a risk factor for febrile seizure.

Conclusion: Anaemia is a common problem in children so treating or preventing anaemia may decrease the prevalence of febrile seizure and also treating hyponatremia may further bring down the episodes of febrile seizures.

Keywords: Fever, Haemoglobin, Iron deficiency

INTRODUCTION

Febrile seizures are the most common cause of seizures in children, occurring in 2-5% of children [1]. A simple febrile seizure is generalised, tonic clonic which usually occurs within 24 hours of onset of fever and it is usually a single episode which lasts for few seconds but may rarely extend up to 15 minutes and is followed by a brief period of post-ictal drowsiness [2]. It occurs between 6 months to 5 years of age without any evidence of neuroinfection, with a peak incidence of febrile seizure around the age of 18 months [3]. Risk of recurrence in febrile convulsions is 30-40% and half of these go on to get a second recurrence [4].

Iron deficiency anaemia is very common among children of less than 4 years which overlaps with the high incidence of simple febrile seizure in age groups of 14 to 18 months in

developing countries with an iron deficiency prevalence of 46 to 66% of children [5-7]. Iron is required for myelination, energy and metabolism of neurotransmitters. Cytochrome C oxidase, a marker of neuronal metabolic activity is decreased in iron deficiency anaemia [5] and also lower seizure threshold levels are seen in children with low serum ferritin levels [6-10].

Iron deficiency anaemia is the most common preventable and treatable condition worldwide [11]. Many studies have suggested iron insufficiency as a predisposing factor for febrile seizures whereas some have described higher haemoglobin and also lower incidence of febrile seizure with low iron levels among febrile seizure cases vs. controls [10,12-17]. Keeping in view the difference of opinion, the study was conducted to find the prevalence of anaemia in simple febrile seizures in this part of Karnataka (Hassan).

The children with recurrent febrile convulsion within the same febrile illness during routine electrolysis were found to have low sodium levels and this relative hyponatremia may trigger the febrile child to develop recurrent febrile seizures [18-20].

Acute hyponatremia can lead to oedema and herniation of brain with neurological symptoms, being evident when serum sodium approaches 120 mEq/L. The severity of cerebral oedema and neurological symptoms are directly related to severity of hyponatremia and less frequently induced by chronic than by acute hyponatremia [21,22].

Sodium is an important electrolyte which plays an important role in cell physiology, depolarisation of neurons, production of electrical discharge and finally occurrence of seizures [23].

Since anaemia and hyponatremia are known to be associated with simple febrile seizures, it is important to know whether there is any correlation between them. Till date there are no studies to show the correlation between anaemia and hyponatremia in simple febrile seizures. Hence, we have done this study to know the correlation between anaemia and hyponatremia in children with simple febrile seizures.

In this study, hyponatremia was defined as serum sodium of <135 meq/L [24]. Children were said to be anaemic if Hb% was <10.5 gm/dL in children aged 6 months to 2 years and <11.5 gm/dL in children aged 2 years to 6 years [25].

MATERIALS AND METHODS

The cross-sectional study was conducted in the department of Pediatrics, Sri Chamarajendra Hospital, Hassan Institute of Medical Sciences, Hassan from November 2013 to November 2015. The children belonging to the age group of 6 months to 5 years presenting to the emergency department with fever and history of seizures were considered for the study.

Patients with evidence of CNS infection and CNS malformation, metabolic causes other than low sodium levels, epilepsy, and atypical febrile seizures patients previously diagnosed with haemolytic anaemia, bleeding or coagulation disorder, haematological malignancies, children on iron supplementation and very sick children were excluded from the study.

After obtaining Institutional Ethical Committee clearance (IEC-76) from the institution, data was collected by taking an informed consent by parents after explaining the purpose of study.

A detailed history including duration of fever, time of onset of seizures, duration of seizures, and family history of seizures were recorded. The history regarding trigger for febrile episode like cough, cold, ear discharge, burning micturition or crying during micturition were recorded. The children from rural and urban areas and their socio-economic status were included in the study.

Vitals i.e. temperature, heart rate, respiratory rate were recorded and the temperature was recorded in axilla for 3 minutes in all the children by using mercury thermometer.

The blood investigations done for anaemia were complete blood count which includes haemoglobin level, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, red cell distribution width using Transasia automated analyser by electronic impedance method and type of anaemia analysed by peripheral smear study by manual examination.

Serum sodium, potassium, calcium were analysed by serum electrolytes using Transasia automated analyser by ion selective electrode method.

STATISTICAL ANALYSIS

Data was entered into excel spread sheet and was analysed with SPSS version 21.0 and interpreted by using descriptive statistics. X2 test of significance was used to find association of simple febrile seizures with anaemia and Hyponatremia.

RESULTS

There were 120 children with history and examination suggestive of simple febrile seizures selected for the study, out of which sixty four (53.3%) were males and fifty six (46.6%) were females. Majority of children having febrile seizures were between 6 months to 2 years of age (61.6%). Most of the children were from rural areas with low socioeconomic background and 32 (27%) children had family history of febrile seizures [Table/Fig-1].

	Variables	Numbers (Percentage)
Sex	Male	64 (53.3)
	Female	56 (46.6)
Age	6 months-2 years	74 (61.6)
	2 years-5 years	46 (38.3)
Place	Urban	28 (23)
	Rural	92 (77)
Family history of seizures	Yes	32 (27)
	No	88 (73)
Socio economic class status	Class I	06 (5)
	Class II	13 (11)
	Class III	28 (23)
	Class IV	73 (61)
Anaemia (60)	Male	30 (50)
	Female	30 (50)
Hyponatremia(43)	Male	28 (65)
	Female	15 (35)

[Table/Fig-1]: Showing Demographic variables of simple febrile seizures.

The study showed 60 (50%) children were having anaemia of which 43 cases were between 6 months to 2 years of age. There was a significant association between anaemia and febrile seizures $p < 0.02$ [Table/Fig-2]. Among those 60 anaemic children 45 children had microcytic hypochromic anaemia and 15 children had normocytic normochromic blood picture.

Febrile seizures	Anaemia		Total
	Yes	No	
Yes	30	34	64
No	30	26	36

[Table/Fig-2]: Showing Association between anaemia and simple febrile seizures.
 $\chi^2=0.535$; $df=1$; $p < 0.02$

In the study, we found 43 (35.8%) children out of 120 were having hyponatremia which was statistically significant ($p < 0.005$). The study also showed 29 children were between the ages of 6 months to 2 years of age having hyponatremia. The study also showed that 37 (30.80%) children were having recurrent febrile seizures of which 18 (48.6%) had anaemia and 16 (43.2%) had hyponatremia [Table/Fig-3,4].

We found a statistically significant ($p < 0.001$) [Table/Fig-5] association between anaemia and hyponatremia in febrile seizures.

Age	Male	Female	Total
Anaemia			
6 months-2 years	19	24	43
2 years-5 years	11	06	17
Hyponatremia			
6 months to 2 years	21	8	29
2 years-5 years	7	7	14

[Table/Fig-3]: Showing age and sex wise distribution of anaemia and Hyponatremia in children.

Febrile seizures	Hyponatremia		Total
	Yes	No	
Yes	28	36	64
No	15	41	56

[Table/Fig-4]: Showing association between hyponatremia and simple febrile seizures.
 $\chi^2=3.7$, $df=1$, $p=0.05$

Hyponatremia	Anaemia		Total
	Yes	No	
Yes	40	03	43
No	20	57	77
			120

[Table/Fig-5]: Showing association between anaemia and Hyponatremia among simple febrile seizures patients.
 $\chi^2=55.6$; $df=1$; $p \leq 0.001$

DISCUSSION

The study was conducted on 120 children with febrile seizures, which revealed 61.6% were under the age of group of 2 years and also showed higher incidence of febrile seizures in males, which was similar to various studies [26-28].

The present study showed 60 out of 120 children (50%) had anaemia. The present study revealed 71% of children with febrile seizures were under the age of 2 years had anaemia whereas, the study done by Bidabadi E et al., it was 44% [16]. Similar study done by Kumari PL [12] in Thiruvanthapura, Kerala showed highly significant association between iron deficiency and simple febrile seizures ($p < 0.001$). The study done by Vaswani RK in Mumbai showed similar results, hence febrile seizures and anaemia were both seen more commonly in children less than 2 years of age which makes the children under 2 years of age at risk for febrile seizures [14].

Among the total anaemic cases, 45 children had microcytic hypochromic anaemia accounting to 37.5% of total number of febrile seizures cases which is comparable to the studies done by Srinivasa S et al., and Sherjil A et al., where it was 40% and 31.8% respectively [29,30]. In our study, a statistically significant ($p < 0.02$) association between anaemia and febrile seizures was found. A study done in Mumbai, India by Vaswani RK et al., found significantly ($p=0.003$) low levels of serum iron [14]. Similar results with high incidence of anaemia in febrile seizure cases were reported by Dawn SH too [31].

Electrolyte imbalance disturbances are known to cause seizure episodes, in the index study we found 43 children with Hyponatremia had febrile seizures which accounts for 37.5% of the total febrile seizure cases which was statistically significant ($p < 0.005$). A study conducted in Karnataka among cases of febrile seizure found that 28.7% had hyponatremia which was statistically significant [32]. Similar studies done by Park SY and Hugen CA et al., also found higher incidence of hyponatremia among febrile seizure cases, 44% and 52% respectively [33,34].

Among the total children admitted with febrile seizure 37 (30.8%) had a history of febrile seizures which was comparable to the study done by Hugen CA et al., and Nadkarni J et al., where it was 28% and 30% respectively [34,35].

Among 120 children selected for the study, 43 children had hyponatremia of which 40 cases also had anaemia which was statistically significant ($p \leq 0.01$). The present study showed anaemic children were more prone to develop Hyponatremia during the episodes of febrile seizures. There is no literature available till date to show how anaemic children were more likely to develop hyponatremia during febrile seizure episode; hence further studies are required in this regard.

LIMITATION

There was no control group and confirmation of iron deficiency anaemia was not done by serum ferritin levels.

CONCLUSION

Prevention of anaemia or decreasing the prevalence of anaemia may decrease the prevalence of febrile seizures in children hence routine screening is required for children. Hyponatremia may predispose the febrile child to simple febrile seizures.

REFERENCES

- [1] Johnston MV. Seizures in childhood, In: Kleigman RM, Behrman RE, Jenson HB, and Stanton. BP. Nelson Text Book of Paediatrics 18th edition Philadelphia: Saunders Elsevier; 2007. P.2457-58.
- [2] Mohamad A, Mikati MA. Seizures in childhood: Kliegman, Behrman, Jenson, Stanton. Nelson text book of paediatrics 19th edition volume 2 Saunders Elsevier, 2013.
- [3] Steering committee on quality improvement and management; Subcommittee on febrile seizures Consensus statement febrile seizures: American Academy of Pediatrics Febrile seizures: clinical practice guidelines for the longtime management of the child with simple febrile seizures, Paediatrics. 2008;121:1281-86. [pubmed] [Google Scholar]
- [4] Vestergaard M, Basso O, Henriksen TB, Osergaard JR, Olsen J. Risk factors for febrile convulsions. *Epidemiology*. 2002;13(3):282-75.
- [5] Hartfield DS, Tan J, Yager JY, Rosychuk RJ, Spady D, Haines C. The association between iron deficiency and febrile seizures in childhood. *Clini Pediatr*. 2009;48:420-26.
- [6] Assessing the iron status of populations: including literature reviews: report of a Joint World Health Organisation/Centre of Disease Control and prevention Technical Consultation on the Assessment of Iron Status at the Population Level, Geneva, Switzerland. 2004:63.
- [7] Sudhagandhi B, Sundaresan S, William WE, Prema A. Prevalence of anemia in the school children of Kattankulathur, Tamilnadu, India. *Int J Nutr Pharmacol Neurol Dis*. 2011; 1:184-88.
- [8] DeUngria M, Rao R, Wobken JD, Luciana M, Nelson CA, Georgieff MK, et al. Perinatal iron deficiency decreases cytochrome c oxidase activity in selected regions of neonatal rat brain. *Pediatric Research*. 2000;48:169-76.
- [9] Pisacane A, Sansone R, Impagliazzo n, Coppola A, Rolando P, D'Apuzzo A, et al. Iron deficiency anemia and febrile convulsion; case control study in children under 2 years. *BMJ*, 1996; 313:314.
- [10] Daoud AS, Batieha A, Abu-ekteish F, Gharaibeh N, Ajlouni S, Hijazi S, et al. Iron status: a possible risk factor for the first febrile seizure. *Epilepsia*. 2002;43(7):740-43.
- [11] World Health Organisation. Iron Deficiency Anemia. Assessment, Prevention and Control. A Guide for Programme Managers. WHO/NHD/013; Geneva: 2001.
- [12] Kumari PL Nair MK, Nair MK, Nair SM, Kailas L, Geetha S. Iron deficiency as risk factor for simple febrile seizures: A case control study. *Indian Pediatr*. 2012;49:17-19. (Pub Med) (Google Scholar).
- [13] Naveed-Ur-Rehman. Biloo AG. Association between iron deficiency anaemia and febrile seizures. *J Coll Phy Sur Pak*. 2005;15(6):338-40. (Pub Med).
- [14] Vaswani RK, Dharaskar PG, Kulkarni S, Ghosh K. Iron deficiency as a risk factor for febrile seizure. *Indian Pediatr*. 2010;47(5):437-39. (PubMed).
- [15] Kobrinsky NL, Yager JY, Cheang MS, Yatscoff RW, Tenenbein M. Does iron deficiency raise the seizure threshold? *J Child Neurol*. 1995;10(2):105-09.
- [16] Bidabadi E, Mashouf M. Association between iron deficiency anemia and first febrile convulsion: a case control study. *Seizure-European Journal of Epilepsy*. 2009;18(5):347-51.
- [17] Talebian NM, Mosavi GA, Khojasteh MR. Relationship between febrile seizure and anaemia. *Iran J Pediatr*. 2006;16:79-82. (Google Scholar).
- [18] Kirivanta T, Airaksinen EM. Low sodium levels in serum are associated with subsequent febrile seizures. *Acta Paediatr*. 1995; 84:1372-74.
- [19] Heydarian F, Ashrafzadeh F, Cam S. Simple febrile seizure: the role of serum sodium levels in prediction of seizure recurrence during the first 24 hours. *Iran J Child Neurology* 2009;3(2):31-34.
- [20] Sakha K, Barzgar M, Evaluation of serum sodium and ionised calcium levels in febrile convulsions. *Med J Tabriz Univ Med Sci*. 2005;27:43-46.
- [21] Androge HJ, Madias NE. Hyponatremia. *N Engl J Med*. 2000; 342:1493-99.
- [22] Bhardwaj A. Neurological impact of vasopressin dysregulation and hyponatremia. *Ann Neurol*. 2006;59:229-36.
- [23] Moritz ML, Ayus JC. Disorders of water metabolism in children: hyponatremia and hypernatremia. *Pediatr Rev*. 2002;23(11):371-79.
- [24] Larry & Greenbaun, *Electrolyte and Acid-Base Disorders: Kleigman, Behrman, Jenson, Stanton, Nelson Text Book of Pediatrics 18th edition, Saunders Elsevier; page 275.*
- [25] OP Ghai, Vinod K Paul, Arvind Bagga; Ghai Essentials Pediatrics, 7th edition; Newdelhi, CBS Publisher and distributor private limited, 2009, Chapter17, Febrile convulsion: page 528.
- [26] Pedspan L. Febrile seizure. *Arch Pediatr*. 2007;14(4):394-98.
- [27] Carmant L Nathalie T;. Febrile convulsion in children. *Epilepsy Res Treat*; 2012. p. 81-89
- [28] Miri Aliabad G, Khajeh A, Safdari L. Clinical, Epidemiological and Laboratory Characteristics of Patients with Febrile Convulsion. *J Compr Ped*. 2013;4(3):134-37.
- [29] Srinivasa S, Reddy SP. Iron deficiency anemia in children with simple febrile seizures. A cohort study: *curr Pediatr Res*. 2014; 18(2):95-98.
- [30] Sherjil A, US Saeed Z, Shehzad S, Amjad R. Iron deficiency anemia- a risk factor for febrile seizures in children; *J Ayub Med Coll Abbottabad* 2010; 22(3):71-73.
- [31] Dawn SH, Joatan T, Jerome Y, Don S. The association between iron deficiency and febrile seizures in childhood. *Clin Pediatr*. 2009;48:420-26.
- [32] Penta VBT, Lakkappa L. Assessment of serum sodium levels among the febrile seizures children in a tertiary care hospital, *Indian J Child Health*. 2018;5(11):670-73.
- [33] Park SY, Lee SJ. The clinical significance of serum sodium concentration in febrile convulsion. *Korean J Pediatr*. 1998;41:1262-67.

[34] Hugen CA, oudesluys-murphy AM, Hop WC. serum sodium levels and probability of recurrent febrile convulsions. Eur J Pediatr. 1995;154(5):403-35.

[35] Nadkarni J, Binaykiya I, Sharma U, Dwwivedi R. Role of serum sodium levels in prediction of seizures recurrence within the same febrile illness; Neurology Asia. 2011;16(3):195-97.

AUTHOR(S):

1. GN Bharat kumar
2. BS Srinivasa
3. SK Manuprakash
4. Ara Syeda Saltanat
5. HR Suma

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Hassan Institute of Medical Sciences, Hassan, Karnataka, India.
2. Assistant Professor, Hassan Institute of Medical Sciences, Hassan, Karnataka, India.
3. Associate Professor, Hassan Institute of Medical Sciences, Hassan, Karnataka, India.
4. Senior Resident, Hassan Institute of Medical Sciences, Hassan, Karnataka, India.

5. Professor and Head, Hassan Institute of Medical Sciences, Hassan, Karnataka, India.
6. Senior Resident, Hassan Institute of Medical Sciences, Hassan, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. BS Srinivasa,
Assistant Professor, 73, 7th Floor, Doctors Quarters,
HIMS, Hassan, Karnataka-573201, India.
E-mail: Srinivasabindu76@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS:

None.

Date of Publishing: Apr 01, 2019