

## STUDY OF ASSOCIATION BETWEEN IRON DEFICIENCY ANEMIA AND FEBRILE SEIZURES

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**ABSTRACT: OBJECTIVE:** To Study the association between Iron deficiency and Febrile seizures in children of age group 6 months–60 months. **MATERIAL AND METHODS:** The Present study is case-control study, done in the department of Paediatrics, Rangaraya Medical College, Govt. General Hospital, Kakinada. 150 Children of age group 6 months – 60 Months (75 Children as study group/ 75 children as control group) were included in the study. Children with Febrile Seizures were considered as study group and febrile illness without seizure as control group, as per inclusion and exclusion criteria. Detailed history was taken from parents and clinical examination findings were recorded investigations like haemoglobin estimations, serum ferritin level were done to all children and specific investigations like CSF analysis, EEG, CT Brain etc. were done according to the need. **RESULTS:** The present study includes 150 children out of which the prevalence of Iron Deficiency anaemia (Hb $\leq$ 11gm/dl) with Febrile seizures is 84% (63 out of 75 children) and in control group 65% (49 out of 75 Children) P Value is 0.0005 which is significant. Prevalence of low ferritin levels ( $\leq$ 30ng/ml) in study group is 58.6% and in control group 30%. The incidence of febrile seizures more common in male children 59% compared to female children 41%. Respiratory tract infections constituted the major cause of fever in both groups. **CONCLUSION:** There is strong positive correlation between haemoglobin concentration and development of febrile seizures (P 0.0008). There is strong positive correlation between low serum Ferritin levels and development of Febrile Seizures (P 0.0005).

**KEYWORDS:** Febrile illness, Febrile Seizures, Serum Ferritin, Malnutrition.

**INTRODUCTION:** Malnutrition is a silent emergency. Iron Deficiency Anaemia is currently the wide spread micronutrient deficiency and affects nearly 1.5 billion people globally. Infant's, Preschool children and women at child bearing age are at greater risk. About 1/3<sup>rd</sup> of World's population suffers from Iron Deficiency Anaemia and of which 90% lives in Third world countries.

Iron Deficiency Anaemia develops when the supply of Iron is insufficient for the requirement of Haemoglobin synthesis.<sup>1</sup> Iron Deficiency results from an imbalance between the sum of the infant's iron endowment at birth plus subsequent intake and the sum of the Infants need for growth and replacement of losses.<sup>2</sup>

WHO Criteria for Iron Deficiency Anemia <sup>3</sup>	
Age Group	Hb%gm/dl
6 Months – 5 Years	$\leq$ 11
5 Years – 11 Years	$\leq$ 11.5
12 Years – 13 Years	$\leq$ 12.0

Table 1

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Normally about 80% – 90% of the Iron that enters in to cells is taken up by the mitochondria and is incorporated into hemoglobin.<sup>4</sup>The chemical form of mitochondrial iron is not known but it does not appear to be ferritin.<sup>5</sup>

Reticuloendothelial system will maintain a seizable storage pool in the form of ferritin and hemosiderin. Hemosiderin is more stable and less available storage form than ferritin.<sup>6</sup> Iron is cofactor for many enzymes like cytochrome, catalase, peroxidases which carry out vital functions in the body.<sup>7</sup> Iron is transported as transferrin and enters the brain endothelial cells.<sup>8</sup> Clinical features includes easy fatigability, exertional dyspnoea, palpitation, giddiness etc.<sup>9</sup> Anaemia is best investigated by the hemoglobin estimation, peripheral smear and hematocrit levels. Iron deficiency is specifically estimated by serum Ferritin,<sup>10</sup> Serum Iron, Total Iron Binding capacity, Red Cell protoporphyrin levels, Bone marrow iron stores and transferrin receptor protein. In iron depletion there will be few or no sideroblasts in reticulo endothelial system.<sup>11</sup>

Febrile convulsions are occasional seizures associated with fever without evidence of intracranial infection or other definable causes; it must be distinguished from epilepsy, which is characterized by recurrent non febrile seiuzures.<sup>12</sup> Fever with febrile seizures mostly caused by respiratory tract infection, otitis media, pneumonia, gastroenteritis, UTI etc. The high rate of seizures with shigellosis and salmonellosis is due to toxaeic effect.<sup>13</sup> Seizures following immunization are seen mainly with pertussis and measles vaccine.<sup>14</sup>

EEG changes more common in children with abnormal neurological signs. Neuroimaging is not indicated unless neurological abnormalities are present.

**MATERIAL AND METHODS:** The Present study is case-control study, done in the department of Paediatrics, Rangaraya Medical College, Govt. General Hospital, Kakinada, over a period of 1 Year from October.' 2010 to September.' 2011. 75 Children of age 6 months–60 months with febrile seizures were taken as study group and 75 children of same age and sex with febrile illness without seizures were taken as control group. Febrile illness group includes respiratory tract infections, gastroenteritis, otitis media etc. Excluding criteria include history of non-febrile seizures, CNS infections, developmental delay, neurological deficits, haemolytic anaemia, bleeding disorders, Hematologic malignancy, those who were on iron supplementation and very sick children.

Haemoglobin level $\leq$ 11gm/dl and serum ferritin level  $\leq$ 30ng/ml taken as per WHO guidelines. Febrile Seizure is a seizure occurring in association with a febrile illness in the absence of CNS infections or any other defined cause of seizure.

Detailed history was taken from parents and thorough clinical examination was done and investigations like haemoglobin estimations, serum ferritin level were done to all children and other investigations like CSF analysis, EEG, CT Brain etc. was done whenever necessary.

Haemoglobin estimation was done by Sahli's Hemoglobinometer, Serum Ferritin estimation was by CLIA Test (Chemi Luminescence Immune Assay) method.

**RESULTS:** The Prevalence of cases of 'febrile seizures with iron deficiency anaemia' was 84% in study group in contrast to 65% in control group (P-Value is  $<0.0008$  which is significant). The prevalence of Febrile seizures with low serum ferritin levels was 58% (P-Value  $<0.0005$ ).

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### DISTRIBUTION OF HB LEVELS IN THE STUDY & CONTROL GROUPS:

Group	Hb		P- Value
	≤11gm/dl	>11gm/dl	
Study	63(84%)	12(16%)	0.0008
Control	49(65%)	26(35%)	

Table 2

### SERUM FERRITIN LEVELS IN STUDY & CONTROL GROUPS:

Group	Ferritin		P- Value
	≤30ng/ml	>30ng/ml	
Study	44(58.6%)	31(41.3%)	0.0005
Control	23(30%)	52(70%)	

Table 3

### DISTRIBUTION OF CASES ACORDING TO NUTRIONAL STATUS:

PEM Grades	Normal	Grade - I	Grade - II	Grade - III	Grade - IV	P- Value
Study Group	43	17	10	4	1	0.017
Control Group	42	29	2	2	0	

Table 4

Out of 75 cases in study group 32 children were malnourished (P-Value 0.017).

Out of 75 Children in study group, 8 children (10.66%) had family history of seizures compared to 1 child (1.33%) in control group with P-Value 0.033 which is significant. In study group Febrile seizures with iron deficiency anaemia was more in male children 59% (44 out of 75) compared to female children 41% (33 out of 75). In the present study, respiratory infections constituted the major cause of fever in both groups (40 children is study and 45 children in control group). EEG showed no significant difference.

**DISCUSSION:** Iron Deficiency is found to be a significant risk factor for Febrile seizures in children of age group 6 months to 5 Years in our study (P 0.0008). In our study 84% (63 out of 75 in study group) had Hb%≤11gm/dl when compared to 65% (49 out of 75 in control group). The mean Hb Percentage in study group was 9.12gm/dl.

Serum Ferritin levels ≤30ng/ml in study group were 58.6% (44 out of 75) compared to control group 30% (23 out of 75) P-value 0.0005. There was statistical significance in the association between nutritional status and the occurrence of febrile seizure (P-Value 0.017). Male children were more prone to Febrile seizures with Iron Deficiency Anaemia (59%) when compared to Female children (41%).

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### VARIABLES IN DIFERANCE STUDYS: RESULTS:

Sl. No.	Variables taken in each study	Panigrahi et al. <sup>15</sup> (ASRAM Eluru study)	Leela Kumari, MKC Nair et. Al <sup>16</sup> (Kerala study)	Rajwanti K Vaswani et al. <sup>17</sup> (Mumbai study)	Azhr Daud et al. <sup>18</sup> (Jordan study)	Present study
1	No. of Cases	35	154	50	75	75
2	Age Group	6 Mo. - 6Yrs	6Mo. - 3Yrs	6Mo. - 6Yrs	6Mo.-6Yrs	6 Mo. - 5Yrs
3	No. Children with Hb≤ 11 gm/dl Study	27(77%)	98(63.6%)		26(35%)	62(82%)
4	Mean Hb (gm/dl) Study	9.6	9.4	9.4	10.65	9.12
5	No. of Children with Serum Ferritin (≤ 30 ng/ml) Study	1129.5%)	98(63.6%)	34(68%)	49(65%)	44(58.6%)
6	Mean Serum Ferritin Study	24.1	46.5	31.9	29.5	49.16

Table 5

In a similar study by Daoud et al, 75 Children with febrile seizures were compared with 75 controls. Mean Ferritin levels were significantly less in study group with febrile seizures 29.dng/ml than in the controls 53.3ng/ml with P 0.0001 proportion of subjects with serum Ferritin level≤30bg/ml was significantly higher among children with febrile seizures (49 of 75 wa 24 of 75) than in controls. Mean levels of Hb, MCV, MCH were also less among febrile seizure group, but differences failed to attain statistical significance.

Similar observations were made in the study by Vaswani et al, from Mumbai. 50 study and 50 controls between 6 months–6 Years age group children were enrolled in the study. Iron deficiency was determined by estimation of Hb and serum Ferritin. The mean serum Ferritin level was significantly low in study (31.9±31.0)ng/ml as compared to controls (53.9±56.5)ng/ml with (P 0.003). The proportion of children with Ferritin≤30ng/ml was significantly higher (P<0.0001) in study (n34, 68%) than in controls (n15, 30%). It was observed that amongst study, 77% had no PEM, 15% grade 1 PEM, and 8% grade II PEM. Whereas within controls 60% has no PEM and 40% had grade I PEM.

Similar observations were made in the study done by Leela Kumari et al, from Kerala where 154 study and 154 controls were included in the study. Children in the age group 6 months – 3 Years presenting with febrile seizures were included in the study group.

No significant difference was noted in the age and gender distribution, and socio-economic status in study & control groups. 63.6% of study & 24.7% of control groups had iron deficiency.

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Variables found to be significantly associated with febrile seizures on univariate analysis included iron deficiency (P 0.001), family history of febrile seizures in first-degree relatives (P 0.004) and family history of epilepsy in first-degree relatives (P 0.004).

A similar prospective case control study was done in Asram Medical College, Andhra Pradesh by Panigrahi et al. In the study group 77% children had Hb $\leq$ 11gm/dl with mean Hb 9.6 $\pm$ 1.78; in the control group 48% children had Hb $\leq$ 11gm/dl with mean Hb 11.7 $\pm$ 1.42. In the study group 29.5% children had serum Ferritin $\leq$ 30ng/ml with mean serum Ferritin level was 24.1ng/ml vs 9% children were having low serum Ferritin level with a mean of 58.9ng/ml (P 0.01) in the control group.

Alfredo Pisacane<sup>19</sup> et al from Naples studies the level of Hb, MCV and serum iron and found that in children younger than 2 years, 30% children with febrile seizures had anaemia compared to 14% in the controls.

**CONCLUSION:** There is strong positive correlation between haemoglobin concentration (Hb $\leq$ 11 gm/dl) and development of febrile seizures (P 0.0008). There is strong positive correlation between low serum Ferritin levels ( $\leq$ 30ng/ml) and development of Febrile Seizures (P 0.0005). In our study, 84% have low haemoglobin levels and 30% have low ferritin levels. The prevalence of Febrile Seizures more in male children 59% compared to female children 41%.

Low levels of serum Ferritin may lower the seizure threshold as iron is important for function of various enzymes and neurotransmitters present in CNS. So, Prophylactic Iron Supplementation is must to all children who are anaemic to prevent Febrile Seizures.

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