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IRON DEFICIENCY ANAEMIA AND ITS ASSOCIATION WITH FEBRILE SEIZURE: A CASE CONTROL STUDY

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ABSTRACT **Background:** The most frequent type of childhood seizure condition, febrile seizures, have a very good prognosis. However, febrile seizures may also be an indication of a serious underlying acute infectious condition such septicaemia or bacterial meningitis. Febrile seizures are age dependant and are uncommon before 3 months and beyond 5 years of age. To analyse Iron deficiency Anaemia and Its Association with Febrile Seizure among children between 6 month to 5 years in Gauhati Medical College, Guwahati. Materials and Method: In this study included 6 months to 60 months child admitted in GMCH and sample size was 134 . Result: Majority 43.28% were belongs to 9-11 gm /dl Hb level out of 134 cases. Conclusion: Iron deficiency anaemia may be considered one of the risk factors for febrile seizure in children. Hence, Children with febrile seizure should be investigated and treated for Iron deficiency anaemia.

Introduction:
Febrile seizure are seizures occurring among children, 6 months to 6 years at temperature 38 C (100 F) or higher without CNS infection or any metabolic imbalance. Simple febrile seizures are generalized, tonic Clonic associated with fever, lasting not more than 15 minutes and not recurring within 24 hour. In 2–5% children, it occurs at least one time. Peak .age is 18 months. Simple febrile fits are not associated with increased risk of mortality. There is genetic predisposition with positive family history, in some families, carrying as autosomal dominant trait. However, in most cases, it is polygenic [1]. Iron plays an important role in myelination as well as production and release of several neurotransmitters in central nervous system. Iron deficiency anaemia (IDA), by altering the level of neurotransmitters may lower seizure threshold, eventually contributing to febrile seizure. The objective of the study was to analyse Iron deficiency Anaemia and Its Association with Febrile Seizure among children between 6 month to 5 years in Gauhati Medical College, Guwahati. and find out the association of Socio- demographic profiles with febrile seizure among children between 6 months to 5years [2]. Several studies have been conducted to establish the relationship between IDA and FS but with conflicting results. Hence, the present study was conducted with the aim to evaluate the association of IDA with FS.

Materials and Method: This study was Hospital based case control study and done on Gauhati Medical College and Hospital, an apex institution of Assam. Study Period was One year from August 2021 to July 2022. Study Population was diagnosed cases of febrile seizure cases in the above mention study period and Patients suffering from fever without seizure admitted in the above mention hospital during the study period were taken as controls in 1:1 ratio after matching the age and sex. Inclusion criteria for Cases was Children age group 6 months- 5 years with Fever and seizure. Children admitted more than 48 hours. Parents of the patient give written informed consent. Inclusion criteria for control was Children same age group in GMCH With history of Fever but no seizure. Children admitted more than 48 hours. In this study, all Central nervous system infection like Meningitis, Acute encephalitis syndrome, cerebral malaria. Children in structural lesions and congenital anomalies of the brain. Chronic Seizure disorder, epilepsy presenting with seizures during fever Leave against medical advice (LAMA) cases were excluded and the patients refusing to participate in the study. Leave against medical advice (LAMA) Controls were excluded.

Sample size and sample technique:
As per departmental records of Paediatric ward , GMCH during 2018-2021, till date total number of fever cases of age group 6 to 60 months admitted in Paediatric ward is 700. Out of these, febrile seizure cases comprised of 39.7% .Hence, total number of febrile cases during

period were 278 cases. In view of multiple risk factors being studied , to give an 80% power in a two sided test with 5% alpha error for any factor whose prevalence 39.7% among controls and assuming the associated odd ratios (OR) to be 2.0 and equal number of cases and controls (r=1) ,the minimum sample size calculated to be 134. Thus, sample size of 134 cases and 134 controls was taken. Data shall be collected from Paediatric ward of GMCH for three days in a week till the required numbers of sample size gets completed and using below formula:

$$N = \frac{(r+1)}{r} \frac{P\,(1-P)(Z_\beta + Z_{\frac{\alpha}{2}})^2}{(P_1 - P_2)^2}$$

$Z_\beta = 0.84$, for 80% power, $Z_{\frac{\alpha}{2}} = 1.96$, for 5% level of significance, r = Ratio of the control to cases, P = a measure of variability, P_1-P_2= Effect size = 0.167, P_1= risk of exposure in cases = 0.564, P2=risk of exposure in control, P= P_2 When diseases is rare, P2= 39.7% = 0.397.

Sampling technique: Cases and Controls were selected from Paediatric ward and PICU, Gauhati Medical College & Hospital in the ratio of 1:1 after adjusting for age and sex. Those patients who fulfilled the required criteria and gave consent for the study were interviewed face to face till required sample size was achieved. Socio-demographic variables were Age, Sex, Religion, family type. If Hb level was less than 11 g / dl, it was considered as anaemia. A predesigned and Pre tested interview proforma and hospital case sheet (secondary data) were used. Data analysis was done by appropriate statistical methods. Criteria for significance used in the study was p < 0.05 at 95% confidence interval (C.I).Chi -square test was used for analysis of categorical variables. Odd ratio was calculated for measuring strength of association.

Result: In this study, out of 134 febrile seizure Cases majority i.e. 42.53% belongs to age group of 12-23 months, 23.13% belongs to 24-35 months and 21.64% belongs to age group of 6-11 months. Out of 134 FS Cases, majority 83% were belongs to males and 38.06% were belongs to females and Mean +/- S.D of cases and controls were 26.8+/-20.179 and 26.8+/- 11.43 respectively. . Association between age group and Febrile seizures was found to be statistically significant (p<.0036) and majority 59.70% FS were Hindu and 39.55% were Islam. Out of 134 cases, majority 61.94% were belongs to Nuclear family and 38.06% belongs to Joint family.

Table 1: Distribution Of Febrile Seizure According To Their Age And Sex

AGE	Months	Number (134)	Percentages(100)
	6 -11	29	21.64 %

	12-23	57	42.53%
	24- 35	31	23.13%
	36- 47	05	3.73%
	48- 60	12	8.95%
SEX	MALE	FEMALE	PERCENTAGES (100)
	6- 11	21 (25.30)	08 (15.69)
	12- 23	35 (42.16)	22 (43.18)
	24- 35	16(19.28)	15 (29.41)
	36- 47	O4 (04.81)	01 (01.96)
	48- 60	07 (06.02)	05(09.80)

TABLE 2: Distribution of religion and type of family and febrile seizure

Religion	Number	Percentages
Hindu	80	59.70
Muslim	53	39.55
Christian	03	02.23
Type of family		
Joint family	51	38.06
Nuclear family	83	61.94

TABLE 3: Distribution of haematological indices and Febrile seizures.

Haemoglobin level	Number	percentages
<7 gm /dl	07	05.22
7-9 gm /dl	21	15.67
9-11 gm/dl	58	43.28
11-13 gm/dl	39	29.10
13-16 gm/dl	09	06.71
RBC		
3.0-4.0	17	12.69
4.1-5.0	83	61.94
5.1-6.0	34	25.37
MCV VALUES		
60.0-70.0	27	20.0
70.1-80.0	75	56.0
80.1-90.0	21	16.0
90.1-100.0	11	08.0
MCH		
18.0-22.0	36	26.85
22.1- 24.0	38	28.38
24.1-28.0	43	32.09
28.1-32.0	17	12.68
MCHC		
32.0-34.0	125	93.28
34.1-44.0	09	06.72

In Table 3 show that majority 43.28% were belongs to 9-11 gm /dl Hb level, 29.10% were belongs to 11-13 mg/dl Hb level and 15.67% were belongs 7-9 mg/dl Hb level and 61.94 % were belongs to 4.10 -5.0 RBC level, 25.37% were belongs to 5.1 -6.0 RBC level. Majority 56.0% were belongs to 70.1 - 80.0 MCV level and 08.0 % were belongs to 90.1 - 100.0 MCV level and 32.09 % were belongs to 24.1 -8.0 MCH level and 12.68% were belongs to 28.1 -32.0 MCH level and 93.28 % were belongs to 32.0 -34.0 MCHC level and In Table 4 show that Mean +/- S.D of Hb (26.68 ,+/- 21.57), RBC (44.66 ,+/- 34.27) MCV (33.5,+/-28.44), MCH (33.5 +/- 11.8), MCHC (67.0 ,+/- 82.02). Among 134 cases, 64.18 % belonged to less than 11 gm/dl, 35.82 % belonged to more than 11 gm/dl and while among controls 47.01 % belonged to less than 11 mg/dl, 52.99% belonged to more than 11 gm /dl. Association between Haemoglobin level and Febrile seizures was to be Significant [P = 0.00068, 95% C .I(1.237-3.295)] and association between Red blood cells (RBC), MCHC and Febrile seizures significant.

Table 4: Comparison of haematological profile between cases and controls

Variables	Group	Mean	SD	P- value &Odd ratio
Hb	Cases	26.8	21.59	0.0068 OR =2.019
	Controls	26.8	11.69	
RBC	Cases	44.66	34.27	0.0047 OR=1.672
	Controls	44.66	19.86	
MCV	Cases	33.5	28.44	0.5763 OR= 1.216
	Controls	44.66	20.00	
MCH	Cases	33.5	11.38	0.3281 OR =1.309
	Controls	28.5	13.89	
MCHC	Cases	67.0	82.02	0.0001 OR= 42.508
	Controls	67.0	48.08	

Table4: Relation between Haemoglobin level and Febrile seizures

Haemoglobin	Cases	Controls	P <0.0068 95% C.I (1.237-3.295) χ2= -7.316
<11 gm /dl	86 (64.18)	63 (47.01)	
>11 gm /dl	48 (35.82)	71 (52.99)	
Total	134 (100)	134 (100)	

DISCUSSION:

The present study shows that out of 134 Febrile seizures, majority 42.53% were belongs to 12-23 months, 23.13 were belongs to 24-35 months and 21.64% were belongs to 6-11 months while Fever (Controls) majority 26.1% were belongs to 12-23 months, 25.4% were belongs to 24-35 months and 22.69 % were belongs to 12-23 months and Mean +/- S.D of cases and controls were 26.8+/-20.179 and 26.8, +/- 11.43 respectively. Febrile seizure incidence is strongly related to age, with the highest incidence rates being young children. In this study, we included children aged 6 to 60 months with febrile seizure and found that children with age 12 -23 months at first FS (42.53%) had increased incidence of recurrent FS. Likewise, Nadirah rasyid ridha et.al (2009), revealed that the children having first FS within 18 months of age. Another study by Berg AT et.al, shown that 66 % of children with recurrent FS were less than 18 months (3). A study done by Naveed-ur-Rehm and co-workers found that the mean age for cases was 22.97+/-9.52 months while that for controls was 22.77+/-11.33(5). A study Bidab et.al, show found the patients and controls were 22.86 +/- 12.86 and 21.91 +/- 13.58 months of mean age respectively. In this study, 61.94% belonged to male, and 38.05% belonged to female while among controls 41.79% belonged to male and 58.20% belonged to female. Association between gender and Febrile seizures was to statistically Significant (6). Similarity, Jyoti Agrawal et.al shown that 83% of children with recurrent FS were males and 17 % were females (p = 0.088) (7). Out of 134 cases, 64.18 % belonged to less than 11 gm/d, 35.82 % belonged to more than 11 gm/dl and while among controls 47.01 % belonged to less than 11 mg/dl ,52.99% belonged to more than 11 gm /dl . Association between Haemoglobin level and Febrile seizures was to be Significant. Dr. Lakshmi M.et.al (2020) study found that Female with associated 58.8% iron deficiency were more when compared to males (49.3%). There was a significant association of iron deficiency anaemia with 1, 2 and 3 of febrile seizure association were 27.4%, 53.4% and 80.9% respectively(9). The amount of Hb, MCV, MCH, MCHC and RBC count were significantly higher among the cases with febrile convulsion than the controls. The incidence of iron deficiency anaemia was significantly higher in controls compared with the cases (p<0.016). Islam.et.al (2020) shows that Mean haemoglobin level (9.40 ± 1.25 mg/dl vs. 13.12 ± 2.05 mg/dl), Mean MCV (80.57 ± 6.14 fl vs. 90.79 ± 3.25 fl), and mean MCHC (29.42 ± 2.36 g/dl vs. 32.44 ± 1.89 g/dl) level were significantly higher in control group. Hence, there was a relative iron deficiency state among the cases (4). Likewise, Waheed .N et.al (2012) study found that out of 323 children with febrile seizures 17 (5.3%) were iron deficient. Mean Hb was 11.71+/-1.38 g/dL, mean MCV 78.40 +/- 3.29, mean MCH 27.11 +/- 3.28, and mean ferritin was 66.57 +/- 24.7(11).Islam. K et.al (2020) study found that Febrile seizure is significantly and negatively correlated with haemoglobin, MCV and MCHC signifying and iron deficiency state may predispose to FS. In this study higher level of MCV, MCHC, were protective for FS. There was no significant difference in Hb level and MCV indices between the two group (4).

CONCLUSION: Iron deficiency anaemia was significantly associated with febrile seizure. Hence iron deficiency may be considered one of the risk factors for FS in children. Children with FS should be investigated and treated for IDA. Iron supplements should be prescribed for the children in developing countries where there is high prevalence of IDA as well as in children with other known risk

factors for FS. Further studies are required to determine the underlying pathophysiology of how iron deficiency lowers the seizure threshold. Also, further prospective studies on large population are required to evaluate the association of IDA with FS as well as if iron supplementation can prevent the occurrence of FS.

Ethical clearance: As obtained from the Institutions Ethical Committee, Gauhati Medical college and Hospital, Guwahati Conflict of interest : No conflict of interest.

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