ORIGINAL ARTICLE

IRON DEFICIENCY ANAEMIA AS RISK FACTOR FOR SIMPLE FEBRILE SEIZURES: A CASE CONTROL STUDY

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Background: Febrile fits is common problem in children. Among other risk factors, iron deficiency anaemia is considered as aggravating factor for febrile fits. Iron deficiency anaemia is preventable and treatable disease. The objective of the study was to find out iron deficiency anaemia as risk factor for febrile fits. **Methods:** It was a case control study. Thirty cases of febrile fits were recorded. Control group of 30 cases was taken at the same time with same variables but without febrile fits. Their temperatures and weights were recorded and laboratory haematological parameters haemoglobin, haematocrit, Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Red Blood Count (RBC) and Red Cell Distribution Width values were collected and analysed statistically with SPSS Ver 20.0 **Results:** In case group 21 had haemoglobin <11.0 gm% while in control group 13 cases had haemoglobin <11.0 gm% (Odd Ratio 3.0513 95% CI 1.0533–8.8390) Mean Haematocrit, RBC, MCV, MCH, MCHC and RDW had statistically significant difference between the two groups (p-value <0.05) **Conclusion:** As Iron Deficiency Anaemia is a risk factor for febrile fits, treatment and prevention of iron deficiency anaemia can decrease incidence of febrile fits.

Keyword: Anaemia; Febrile fits; Fits; Children

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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 hours.[1] In 2–5% children, it occurs at least one time. Peak age is 18 months.[1] Simple febrile fits are not associated with increased risk of mortality.[2] There is genetic predisposition with positive family history, in some families, carrying as autosomal dominant trait. However, in most cases, it is polygenic.[2] Its exact pathophysiology is known.[3]

Febrile seizures often occurs in context with of otitis media, roseola, herpes simplex 6, shigella or similar infections.[4] Many independent risk factors (genetic factors, age, gender, fever, type and duration of seizure, family and developmental history, multiple seizures, perinatal exposure to antiretroviral drugs, history of maternal smoking and alcohol consumption during pregnancy) have been studied as potential predictors of recurrent febrile seizures.[5–8] Among these, Iron Deficiency anaemia has been studied and found associated with increased incidence of febrile fits.[9,10] Iron deficiency anaemia is commonest micronutrient deficiency worldwide (30%) especially in developing countries (50%), more prevalent in 6–24 months age.[11–13] As it is preventable cause, incidence of febrile fits can be decreased by treating nutritional anaemia with diet and iron supplements.[13] Iron deficiency reduces the metabolism of some neurotransmitters, such as monoamine and aldehyde oxidase[14–17] and thus it may alter the seizure threshold of a child. In addition, the expression of cytochrome C oxidase, a marker of neuronal metabolic activity, is decreased in iron deficiency anaemia.[18] Iron deficiency is postulated as a risk factor for febrile seizures in children and it is an easily correctable condition.[19] In Pakistan, studies showed iron deficiency anaemia as predisposing factor of increased simple febrile fits.[20–22] So current study was designed to see association of anaemia with febrile fits in our hospital, if any.

MATERIAL AND METHODS

It was a case control study. Permission for this study was taken from hospital ethical committee. Thirty Cases of simple febrile fits were collected out of total 1848 cases, admitted from July to December 2015 in Shaikh Khalifa Bin Zayed Al-Nahyan Hospital/CMH Muzaffarabad. Cases with known epilepsy, complex seizures, CNS infection, mentally retarded and metabolic disorders were excluded.

Age, sex and weight were documented. Diagnosis of simple febrile fits was made after detailed history and examination. Control group of 30 febrile cases with same age and gender but without fits were selected to compare with case

group. Axillary temperature more than 37.8 ^{o}C was considered as fever. Fit lasting less than 15 minutes and not recurring within 24 hour without CNS infection or metabolic imbalance were considered simple febrile fits. Cases in both groups with haemoglobin <11.5 Gm/dl, haematocrit, Decreased Red Blood Cell (RBC), Mean Corpuscle Volume (MCV), Mean Corpuscle Haemoglobin (MCH), Mean Corpuscle Haemoglobin Concentration (MCHC) and increased Red Cell Distribution Width (RCDW) were taken as diagnostic criteria for Iron Deficiency Anaemia. Other causes of anaemia were ruled out through clinical evaluation. Serum Ferritin Level could not be done as this facility was not available in hospital and patients were not able to afford it. SPSS version 20 was used to enter and analyse data. As the sample size was small, Fisher exact test was applied for comparison. *p*-value<0.05 was considered as significant.

RESULTS

Total cases admitted in children ward during study period were 1848, out of which 30 cases (1.6%) documented simple febrile. Control group had also 30 cases for comparison. Matching variables of both groups are shown in table-1. Both the groups were comparable at the base line as shown in the table-1.

In case group 21 had Haemoglobin <11.0 gm% while in control group 13 cases had haemoglobin <11.0 gm% (Odd Ratio 3.0513 95% CI 1.0533–8.8390). Mean Haemoglobin, Haematocrit, Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Red cell Distribution Width (RDW) and Red Blood Cell (RBC) had statistically significant difference between the two groups P value as shown in table-2.

Table-1: Matching variables; case & control group

Variable	Case	Control	*p*-value <0.05
Age (Months)	27.90±14.60	26.97±15.92	0.4065
Sex	Male=17 Female=13	Male=16 Female=14	1.0
Area	Rural=19 Urban= 11	Rural=21 Urban=9	0.7846
Family history of febrile fits	Yes=2, No=28	Yes=3, No=27	1.0
Family history of epilepsy	Yes= 1, No=29	Yes=4, No= 26	0.3532
Weight	10.76±3.03	10.63±2.18	0.4229
Temperature	101.35±1.21	101.12±1.13	0.5732
TLC Count	13567±5942	13226±4626	0.4027

Table-2: Comparing variables; case & control group

Variable	Cases Means & Sd	Control Means & SD	*p*-value (<0.05)
Haemoglobin (Gm%)	10.15±1.37	11.08±0.86	0.001
Haematocrit (%)	31.19±4.1	33.65±2.36	0.002
MCV (fl)	68.82±13.36	74.90±5.09	0.011
MCH (pg)	23.63±3.17	25.32±2.92	0.017
MCHC (Gm/dl)	31.57±2.73	32.80±2.19	0.02
RDW (fl)	49.21±8.1	41.11±3.97	0.004
RBC (Millions)	3.79±0.49	4.08±0.73	0.032

DISCUSSION

Simple febrile convulsions are common among 2–5% of children from 6 months to 5 years.[1] Though it has benign effects on child health but still frightening for parents. Many risk factors like genetic predisposition, gender, age, perinatal exposure to drugs, smoking and alcohol ingestion during pregnancy had been studied[5–8] and Iron Deficiency Anaemia is a major risk factor found aggravating simple febrile fits in many studies[9,10]. Some studies showed protective effects on it[23] and others found no association with simple febrile fits[24]. In Pakistan, studies showed association of iron deficiency anaemia with simple febrile fits as aggravating factor.[20–22]

First time, association of Iron Deficiency Anaemia with febrile fits was studied by Pisacaneet *et al*.[9] In his study, Iron Deficiency Anaemia was significant in febrile fits cases as compared to control cases. In a study done in Bhopal in 2015, done by Shreya Gupta *et al*, 70 children with Febrile Seizures showed significant low Hb (<11 Gm/dl) as compared to 100 children in control group. Fallah *et al* from Iran showed low Mean HB (11.46±1.18 gm/dl) in case group as compared to control group (11.9±0.89 gm/dl) which was significant.[25] Similarly in a Pakistani study done in Abbottabad in 2013 by Ambreen Sultan *et al* 68% had low Hbin 31 children with febrile fits as compared to 32% in 31 children with fever but without febrile fits. Our study showed significant low haemoglobin in case group (21/30, 70%) as compared to control group (13/30, 43%) which was significant (*p*-value <0.05). It also showed low mean Hb (10.15±1.37) in 30 children with febrile

fits as compared to mean Hb (11.08±0.86) in 30 children in control group (*p*-value <0.05). It correlates closely with international and national studies.

In our study, other haematological indicators mean Haematocrit, MCV, MCH, MCHC were significantly lower in case group than control group while RcDW was higher in cases than controls, an indicator of iron deficiency anaemia. In Egyptian children, Boshra *et al*[26] showed mean haemoglobin, haematocrit and MCH significant low in simple febrile fits case as compared to control group. Similarly, an Indian study done by Srinivasa *et al*[27] showed low Haemoglobin, MCV, MCHC in febrile fits cases as compared to control (Odd ratio 1.84). In another Indian study done in 2015 by M.S. Raju *et al*[28] haemoglobin <11.0 in cases was 84% while in control groups 65% and this difference was significant.

Some studies showed no association of iron deficiency anaemia with increased risk of febrile fits.[24] In an Iranian study done in 2009 by Salehi Omran MR[29] showed Mean Haemoglobin 11.75±1.15 gm/dl in case group while 11.99±1.94 gm/dl in control group and this difference was not statistically significant. In a met analysis of 8 case control study done by Idro R *et al*[30] in Kenya in 2010, showed iron deficiency anaemia with increased risk for febrile seizures (Odd Ratio 1.79).

CONCLUSION

These results show that anaemia predisposes to febrile fits and if anaemia is treated and prevented well in time, incidence of febrile fits can be reduced.

Limitation: Due to non-availability of Serum Ferritin level test facility in hospital and non-affordability of patient, Serum Ferritin level could not be done.

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AUTHORS' CONTRIBUTION

NA collected data. AGN reviewed literature and KTA analysed data and, wrote results and discussion.

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