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Original Research Article

An observational study on anaemia in children admitted to a tertiary teaching hospital with first episode of febrile seizures

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ABSTRACT

Background: The association between anaemia and iron deficiency anaemia with febrile seizures is still not very well understood. The purpose of this study was to describe the occurrence of anaemia in children admitted with first episode of febrile seizures.
Methods: This was a hospital based prospective study conducted at Central Referral Hospital, Gangtok, Sikkim, India from December 2012 to May 2014 on 50 children in the age group of 6 to 60 months admitted with first episode of febrile seizures. Detailed history and physical examination were performed and findings recorded and complete blood count, serum electrolytes and random blood sugar were done in all children. Mentzer Index was calculated from the haematological data.
Results: The mean age in this study was 24.88±13.22 months. 74% of the cases were males. Twenty-eight children (56%) had anaemia out of which twenty-seven had Iron deficiency anaemia. The statistical analysis of qualitative data using Chi-square test with Yate's correction revealed no statistically significant difference between number of children with anaemia and no anaemia (p value=0.1493) and also between number of children with Iron deficiency anaemia and children with no Iron deficiency anaemia (p value=0.4478).
Conclusions: This study did not reveal a higher occurrence of anaemia as well as iron deficiency anaemia in children admitted with first episode of febrile seizures.

Keywords: Anaemia, Febrile seizures, Iron deficiency anaemia, Mentzer index

INTRODUCTION

Febrile seizures are the most common cause of seizures in childhood in the age group of 6 to 60 months. Racial and geographic variations may be an important determinant in the higher incidence of febrile convulsions in certain population and in developing nations. The signs and symptoms of febrile seizures are well recognized. Some genetic markers of susceptibility to febrile seizures are established, and the proximate trigger of febrile seizures is obvious. Yet, it is still not really understood why certain children and others are affected, how and why fever causes seizures to occur, the best way to prevent or treat febrile seizures and biomarkers to determine which children are at greater risk for later development of unprovoked seizures (i.e., epilepsy).

An important pre-disposing factor for febrile seizures in children has been postulated to be iron deficiency and iron deficiency anaemia.[1] Iron deficiency has been associated with cognitive and neuro-behavioural

disturbances like pica, restless, leg syndrome and breath holding spells.[2] Although numerous studies have been done to establish link between iron deficiency anaemia and febrile seizures, the results are conflicting. It is still not very well understood whether isolated iron deficiency anaemia or anaemia as a whole predisposes children to febrile seizures. This study investigates the presence of anaemia and iron deficiency anaemia in children admitted with first episode of febrile seizures.

METHODS

This study was an observational cross-sectional hospital-based study conducted in the Department of Pediatrics of Central Referral Hospital, Sikkim Manipal Institute of Medical Sciences, a tertiary teaching hospital situated in Gangtok, Sikkim. Gangtok is the capital town of Sikkim. Sikkim is one of the north eastern state of India. The population of Sikkim comprises of three main ethnic communities- Nepalese, Bhutia and Lepchas as well as non-ethnic migrant population. Nepalese are the major ethnic group constituting 70% of the population.

The study was conducted within a period of one and half year from December 2012 to May 2014. The study was approved by the Institutional Research Protocol Committee and Institutional Ethics Committee of SMIMS.

The study group included children aged 6 to 60 months who were admitted to our hospital during the study period with first episode of febrile seizure. The children were diagnosed of having had a febrile seizure if seizure occurred in a neurologically healthy infant and children associated with body temperature of 38ºC or higher without any evidence of intracranial infection or inflammation or acute systemic abnormality as a defined cause and with no history of seizures in the absence of fever. As this was a hospital-based study a critical sample size of 50 was calculated using previous prevalence (p) and 5% absolute allowable error (L) with the formula 4pq/L2.

After stabilization of these children, informed consent was taken from the parents/guardians of the child to include them in this study. A detailed history and physical examination with emphasis on neurological examination was done. After which blood was sent for complete blood count, reticulocyte count, peripheral smear, serum sodium, calcium, random glucose for all children. Other investigations like lumbar puncture, neuroimaging, electroencephalography was done as indicated by standard guidelines. Mentzer index was calculated as Mean Corpuscular Volume (MCV) /Red blood cell count. Anaemia in our study was defined as haemoglobin in g/dl below the normal haemoglobin for age as per WHO criteria. Anaemia was considered to be due to iron deficiency if Mean Corpuscular Volume (MCV) and Mean Corpuscular Haemoglobin (MCH) were two standard deviation below normal for age, Mentzer index >13, RDW more than normal for age and normal leukocyte morphology with normal platelet and low reticulocyte count. The data was collected in Microsoft Excel spread sheet 2010. The descriptive statistics for continuous variables was derived using statistical software – Stats Plus 2009 Professional ® version 5.8.4. Analysis of qualitative/discrete data was done using Chi-Square test with Yate's correction. Level of significance was expressed as p value <0.05.

RESULTS

Fifty children aged 6 to 60 months were included in our study. The mean age in our study group was 24.88 months (±13.22 SD) ranging from 8 to 80 months, with mode of 36 months and confidence interval of 0.05.There were 37 males (74%) and 13 females (26%) in our study. The relative risk for gender was 1.544 with 95% confidence limit. Majority of the children belonged to the Nepali ethnicity (66%), rest of them belonged to the Bhutia (8%), Lepcha (8%) and non-ethnic (18%) population. The highest incidence of febrile seizures in the study group was noted between the months of March and June. Majority of cases in our study group had simple febrile seizures (74%) and 26% had complex febrile seizures. The aetiology of fever in these children is shown in Figure 1.

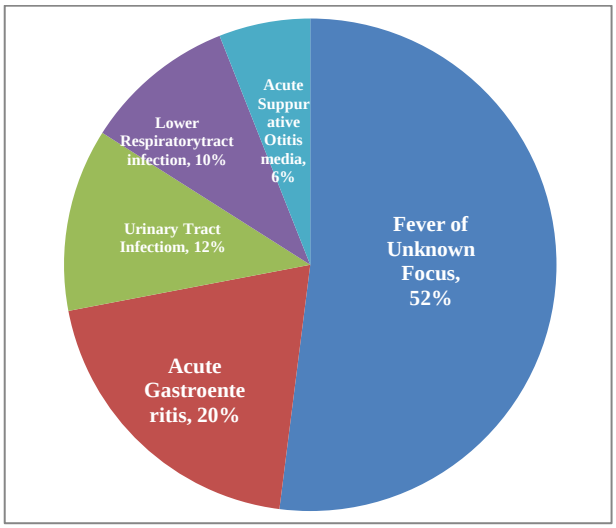

Figure 1: Aetiological profile of fever in the cases of the study group.

Most of the children (82%) had no history of recent vaccination, 9 children had history of recent vaccination. There was positive family history of febrile seizures in 10 children. The descriptive statistics of haematological and biochemical values is given in Table 1.

Out of the fifty children, 28 (56%) children were anaemic. In our study, out of the 28 children with anaemia, 27 (96.4%) had iron deficiency anaemia. The statistical analysis of the difference between the study group in relation to anaemia is given in Table 2.

Table 1: Descriptive statistics of the haematological and biochemical variables.

Parameter	Confidence interval	Mean	Standard deviation	Mode	Maximum value	Minimum value	Range
Haemoglobin	0.05	10.75	1.08	11.1	13	7.9	5.1
Total leukocyte count	0.05	12114.8	5282.99	9800	27800	3800	23900
Mean corpuscular volume	0.05	74.24	5.89	76	85	58	27
Red cell distribution width	0.05	13.52	1.5	14.8	16.8	10.3	6.5
RBC count	0.05	433000	0.37	NA	511000	359000	1.52
Mentzer index	0.05	17.30	2.39	15.95	23.68	12.72	10.96
Sodium	0.05	132.6	3.26	133	137	120	17
Calcium	0.05	9.58	0.60	10	10.5	8.3	2.2
Random blood sugar	0.05	108.8	21.76	98	170	54	116

Table 2: Statistical analysis of the difference between the study groups in relation to anaemia.

Statistical Analysis of Difference in the number of children with anaemia and those without anaemia		
Anaemia	**No Anaemia**	**P value**
28 (56%)	22 (44%)	0.1493
Statistical analysis of difference in the number of children with Iron deficiency anaemia and those without anaemia		
Iron Deficiency Anaemia	**No Anaemia**	**P value**
27 (96.4%)	22 (44%)	0.1478

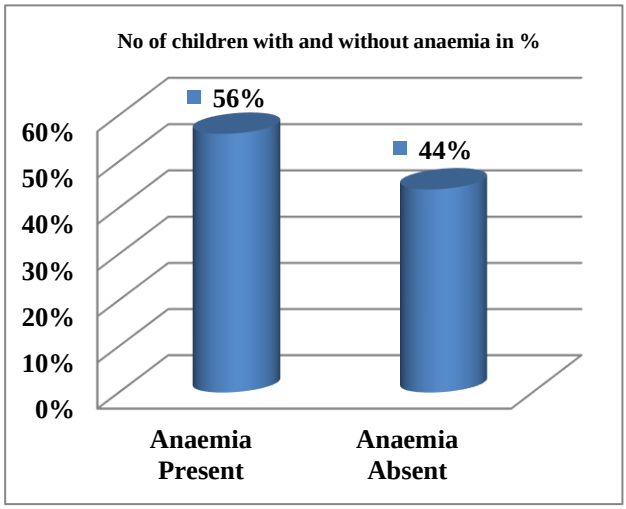

Figure 2: Distribution of anaemia in the study group.

Similarly, the difference between the number of children with iron deficiency anaemia and children without anaemia was found to be statistically not significant by Chi- square test (p=0.4478). The difference between the number of anaemic children and children without anaemia was found to be statistically not significant by Chi- square test (p=0.1493).

DISCUSSION

Around 3 to 4% of children experience at least one episode of febrile seizures by the age of 5 years.[3] Febrile seizures accounts for 6 to 8% of admissions in children aged 6 to 60 months in the hospital where the study was conducted. The mean age of our children was 24.88±13.22 months which is above that seen in both Indian and Western studies on febrile seizures: 1.73±0.94 years (Vaswani et al), 17.6±8.81 months (Leela Kumari et al), 18.9±7.6 months (Kobrinsky et al).[4-6] This can be accounted for by the fact that we included children with febrile seizures brought to medical attention for the first time which need not have been the first episode of febrile seizures. As in Sikkim there is a tendency in the local population to resort to traditional healers for treatment of seizures first, hence the first episode is usually missed. Majority of children in our study group were males (74%) showing a statistically significant difference in the occurrence of febrile seizures as per gender. This is in consensus with other studies which show male preponderance in the occurrence of febrile seizures: 69% and 58%.[6,7] Most of the children belonged to the Nepali community (66%) which is statistically significant in comparison to other ethnicities. However, this result cannot be interpreted as higher risk of febrile seizures in children of Nepali origin as the population of Sikkim comprises of 70% Nepalese. The peak incidence of occurrence of febrile seizures in our study was noted between the months of March to June. This can be accounted by the higher rates of viral infections in children during this season. The commonest aetiology of fever was identified as fever without focus. The other etiologies identified were Acute gastroenteritis (20%), Urinary tract infection (12%) , Lower Respiratory tract Infection (10%), Acute Suppurative Otitis Media (6%). Most of the children recovered from the febrile illness without the use of antibiotics within two to three days and had no further episode of febrile seizures during the hospital stay. This is a known fact that the most common aetiology of fever associated with febrile seizures is fever without localizing signs by respiratory or enteric viral

pathogens. There was no statistically significant association of occurrence of febrile seizure with immunisation. It has been noted that majority of children who had seizures following vaccination had Dravet syndrome mutations. This clearly indicates that their disease is due to mutation and not due to vaccine.[8] 20% of the children had positive family history which is comparable to an Indian study by Leela Kumari, et al (26%) and that by Tsuboi, et al (9-24%).[5,9]

The mean haemoglobin was 10.75±1.09 gm/dl which is comparable to the mean haemoglobin of children with febrile seizures in studies from India and Iran (9.4±1.2 gm/dl- Vaswani et al, 11.46±1.18 gm /dl -Fallah R et al, 10.48±1.16gm/dl- Bidabadi E et al) whereas it is lower than that seen in Western studies (11.95±1.2 gm/dl- Kobrinsky et al).[4,6,7,10] This underlies the importance and higher prevalence of anaemia in developing countries. The mean observed MCV n the study group was 74.24±5.89 fl/dl. It is comparable to other studies: 77.5 ±5.6- Kobrinsky et al, 73.4±9.5 -Vaswani et al, 75.51 ±5.11 -Fallah R et al, 77.54±5.11- Bidabadi E et al.[4,6,7,10] The mean total leukocyte count was 12,114,8±5282.99 /cubic mm which is comparable to study by Kobrinsky et al (14.4±9.3×103/cubic mm).[6] The elevated WBC count seen in febrile seizure is most probably due to stress response and unlikely due to bacterial infection as fever subsided without antibiotics in most of the children. The mean of Mentzer index was 17.3±2.39. The mean serum sodium was 132.62±3.26 mmol/l; mean serum calcium was 9.58±0.60 mg/dl and mean GRBS was 108.8±21.76 mg/dl. These investigations were done to rule out metabolic cause of seizure and aid in emergency management. Most values were found to be in normal range in all fifty children. Most of the results in our study correlate with established data and previous studies therefore can be considered reliable. Twenty-eight children (56%) children had anaemia, out of which most of them (96.4%) had Iron deficiency anaemia. The statistical analysis of qualitative data revealed no significant difference between the number of children with anaemia and children with no anaemia and also between the number of children with Iron deficiency anaemia and children with any anaemia. Hence as per our study both anaemia as well as Iron deficiency anaemia is not more common in children with febrile seizures. Numerous studies done worldwide on Iron deficiency anaemia and febrile seizures have yielded conflicting results. Pisacane et al, in a case control study done on 156 children between the age group of 6-24 months in Italy found anaemia more common in children with febrile seizures but no association with iron deficiency.[1] A similar case control study carried out on 156 cases and 156 controls in South India by Leela Kumari et al, found Iron deficiency anaemia defined as Hb <11g%, Serum Ferritin <12 ng/ml and RDW >15 more in children with febrile seizures.[5] Vaswani et al, in a study in Mumbai found statistically significant lower serum ferritin levels in the febrile seizure group.[4] Similar studies in Iran by Fallah R et al, and Sherjil A et al, in Pakistan found iron deficiency anaemia more in children with febrile seizures.[7,11] However, studies by and Kobrinsky et al, Bidabadi E et al, and Derakhshanfar H et al, showed iron deficiency anaemia significantly lower in children with febrile seizures. The conflicting results seen in different studies done worldwide are probably due to the fact that iron deficiency results in neuro - behavioural alterations rather than seizures.[6,10,12] Seizures have been noted to occur in presence of iron excess in children on parenteral iron therapy or frequent blood transfusions. This is induced by damage due to oxygen free radicals.[6] However we cannot confirm the lack of association between iron deficiency and febrile seizures through our study as we could have missed a considerable number of subclinical cases with early stages of iron deficiency with normal haemoglobin and red cell indices. Moreover, anaemia is the end-point of micronutrient deficiencies and further studies are required to confirm whether the presence of anaemia is a contributing factor or a coincidental finding. The strength of the study was that it was a study done from a geographically isolated region with no previous data on febrile seizures and the use of Mentzer index to identify Iron deficiency anaemia. Although Mentzer index is an established haematological parameter unaffected by inflammation and stress, no previous studies on febrile seizures and anaemia have been carried out using this index.

CONCLUSION

In this study, the number of children with anaemia and iron deficiency anaemia was not statistically different than the number of children without anaemia and iron deficiency anaemia. Hence, anaemia as well iron deficiency anaemia may not be a risk factor for febrile convulsions.

However, this study may have missed children in early stages of iron deficiency. Further studied need to be done on iron deficiency and its association with febrile seizures as it is the commonest micronutrient deficiency in developing countries and is effectively remediable by iron therapy.

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