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Evaluation of Serum Iron in Patients with Afebrile Seizure

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ABSTRACT:

Background : Two hypotheses have been suggested to explain the origin of seizures after brain injury. One suggests that inhibitory neurons are selectively damaged and remaining principal excitatory neurons become hyperexcitable .

Aim : To evaluate the relation between the presence of iron deficiency anemia and the occurrence of afebrile fit.

Patients and method: A case control study done on 40 patients with afebrile seizure attending to the pediatrics department in Samaraa general hospital during the period from first of July to the last of October 2017year.Each patient with afebrile seizure were assessed by prepared questionnaire including ,name, age, sex, residents, pre-ectal, ictal, post-ectal, pica symptom, presence of risk factor and family history of seizure ..Each patient examined for presence of pallor ,chionlychia , angular stomatitis ,flat tongue and organomegally .Each patient included in the study were sent for serum iron. A patient were sent for also EEG and C.T. scan.

Results: Most of the study cases presented with pallor 17 cases (29.31%). Regarding pre-ictal symptom, most of them are abnormal head movement 7cases (14.28%). In ictal-state symptom, most of them had tonic-clonic seizure 8cases (19.51%). In post-ictal state symptom, most of cases had drowsiness 28cases (32.18%). In EEG report, from 22 patients had EEG record, 14 cases (63.62%) were abnormal and diagnosed as having seizure. In C.T Scan report, where a19 patients we're did examination, 9cases (47%) patient were normal. Most of cases had no risk factor for seizure 24cases (60%). Most of cases were between ≥1 yr-<5 yrs.19 cases (47.5%), had low iron. In 40 cases were taken, 22cases (55%) of them were of low iron. of 40 cases of seizure, those with low serum iron 22cases (55%) show that 15cases (37.5%) of patients having uncontrolled seizure and 7cases (17.5%) of patients having control seizure, in comparison to16 (40%) of patients with normal serum iron, 11 cases (27.5%) of them had uncontrolled seizure and 5cases (12.5%) had control seizure.

Conclusion: The study concludes that there was no significant result regarding iron level and seizure occurrence. The study recommended further studies on bigger sample size and for a longer period of time to clarify the occurrence of seizure among the patients with low iron.

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Introduction

A seizure or convulsion is a paroxysmal, time-limited change in motor activity and/or behavior that results from abnormal electrical activity in the brain(1). Seizures are common in the pediatric age group and occur in ≈10% of children. Most seizures in children are provoked by somatic disorders originating outside the brain, such as high fever, infection, syncope, head trauma, hypoxia, toxins, or cardiac arrhythmias. Although the precise mechanisms of seizures are unknown, several physiologic factors are responsible for the development of a seizure. Seizures may arise from areas of neuronal death, and these regions of the brain may promote development of novel hyperexcitable synapses that can cause seizures(1).

Two hypotheses have been suggested to explain the origin of seizures after brain injury. One suggests that inhibitory neurons are selectively damaged and remaining principal excitatory neurons become hyper-excitable. The other hypothesis suggests that aberrant excitatory circuits are formed as part of reorganization after injury. Genetic factors account for at least 20% of all cases of epilepsy (2).

Iron is a well-known element that contained in the structure of several enzymes including brain enzymes, mono amino oxidase inhibitors and some neurotransmitter .The mechanism by which iron deficiency impairs neurologic function is unknown. Many enzymes in neural tissue require iron for normal function .The iron deficient patient develop sever behavioral anomalies, motor in coordination ,and seizures. There was a well known correlation between iron deficiency and febrile convulsion .still the association between iron deficiency afebrile convulsion was conflicting (9,10,11,) .

Aim : Aim : To evaluate the relation between the presence of iron deficiency anemia and the occurance of afebrile fit .

Patient and Methods

A case control study done on 40 patients with afebrile seizure attending to the pediatrics department at Samaraa general hospital during the period from first of July to the last of October 2017year.Each patient with afebrile seizure were assessed by prepared questionnaire including ,name, age, sex, residents, pre-ectal, ictal, post-ectal, pica symptom, presence of risk factor and family history of seizure ..Each patient examined for presence of pallor , chionlychia, angular stomatitis ,flat tongue and organomegally .Each patient included in the study were sent

for serum iron. A patient were sent for also EEG and C.T. scan.

Inclusion Criteria:-

1. Patient with afebrile seizure [first attack or recurrent attack] admitted during the study period.
2. Age more than 4 months age. This is because iron storage is enough for the first 4 month of life even preterm patient.

Exclusion criteria:-

1. Patient less than 4 month of age.
2. Patient with hematological disease like thalassemia or any hematological disease.
3. Patient with fever.
4. Patient on iron supplement.

Results

Figure (1) shows the distribution of study cases and control according to sex, of a total of 40 children with their first attack of a febrile seizure or recurrence (study case group),

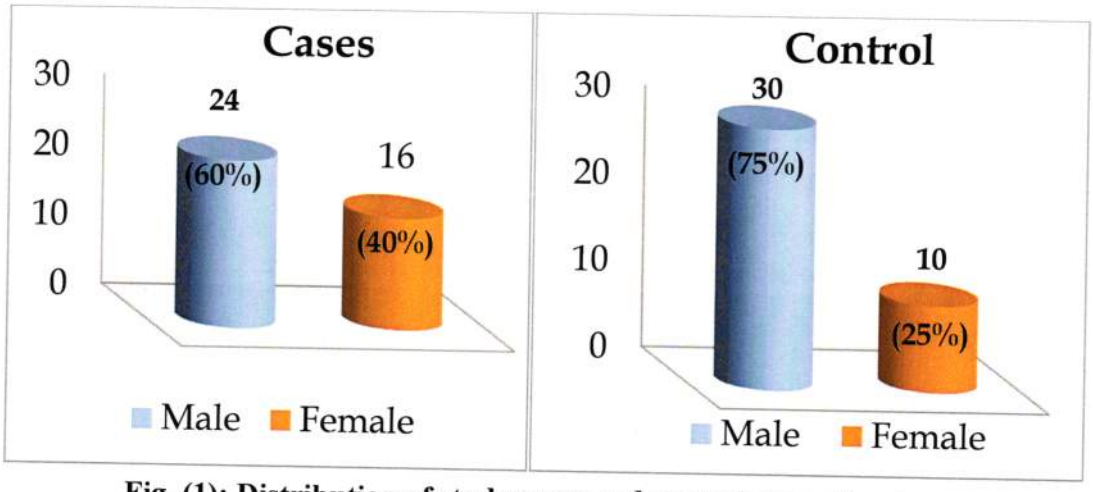


Fig. (1): Distribution of study cases and control according to sex

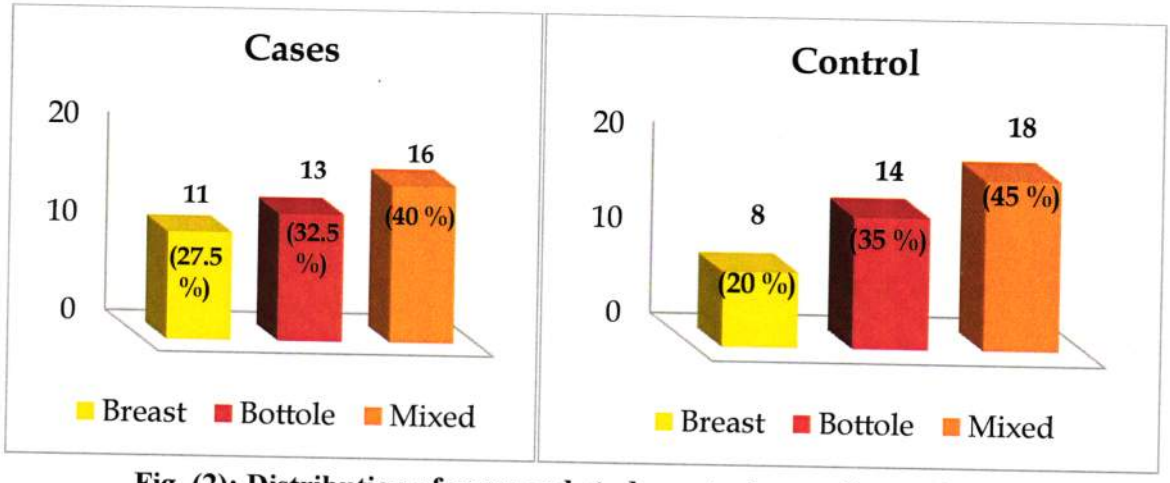
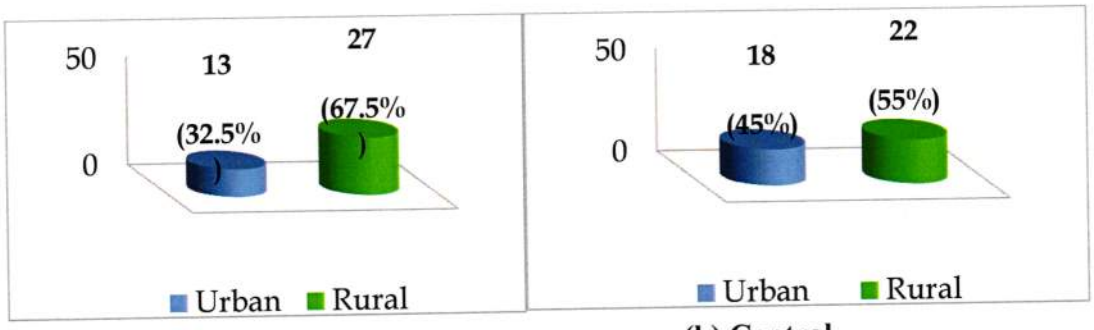


Fig. (2): Distribution of cases and study control according to feeding

Among the study cases group 16 (40%) were mixed feeders, 13cases (32.5%) had bottle feeding and 11cases (27.5%) had breast feeding, while among the control groups, 18 cases (45%) were mixed feeders,14 cases (35%) were bottle feeding, and 8 cases (20%) were on breast feeding, as shown in Fig.(2).

Among the study cases 27 cases (67.5%) were from rural and 13 cases(32%) were from urban areas, while control groups 22 cases (55%)were rural and 18cases (45%) were from urban areas, as shown in Fig.(3).



(a) Cases **(b) Control**

Fig. (3): Distribution of study cases and control according to residence

Regarding of the distribution of study cases and control according to age as given in Table (4.1),

Table (1): Distribution of study cases and control according to age

Age	Cases		Control	
	No.	(%)	No.	(%)
≥ 4 month-<1 yr.	12	30	11	27.5
≥1 yr-<5 yrs.	19	47.5	21	52.5
≥5 yrs.-<10 yrs.	4	10	2	5
≥10 yrs.	5	12.5	6	15
Total	40	100	40	100

P. value = 0.825173 (not significant), df=3

Table (2) shows the distribution of study cases according to clinical picture, most of them had pallor 17 cases (29.31%) .

Table (2): Distribution of study cases according to clinical picture.

Symptom	No.	(%)
Pallor	17	29.31
Anorexia	12	20.68
Angular stomatitis	7	12.06
Pica	5	8.62
Dizziness	5	8.62
Flat tongue	4	6.89
Fatigability	3	5.17
Organomegally	3	5.17
Chionlychia	2	3.44

Table (4.3) shows the distribution of study cases according to pre-ictal symptom, most of them are abnormal head movement 7cases (14.28%) .

Table(3): Distribution of study cases according to pre-ictal symptom

Symptom	No.	(%)
Head movement	7	14.28
Excessive salivation	6	12.24
Fear	5	10.20
Crying	5	10.20
Headache	4	8.16
Vomiting	4	8.16
Hallucination	4	8.16
Lip smacking	3	6.12
Swallowing	3	6.12
Chest discomfort	3	6.12
Disturb vision	3	6.12
Epigastric discomfort	1	2.04
Unpleasant feeling	1	2.04

Table (4) shows the distribution of study cases according to Ictal-state symptom, most of them had tonic-clonic seizure 8cases (19.51%), followed by rolling of eye 6cases (14.63%) and defecation 5cases (12.19%).

Table (4): Distribution of study cases according to Ictal-state symptom.

Symptom	No.	(%)
Tonic –clonic movement	8	19.51
Rolling of eye	6	14.63
Defecation	5	12.19
Urination	3	7.31
Partial seizure	3	7.31
Trauma from falling	3	7.31
Staring	3	7.31
Myoclonic	2	4.87
Tonic	2	4.87
Clonic	2	4.87
Snoring	2	4.87
Tongue bite	2	4.87

Table (5) shows the distribution of study cases according to post-ictal state symptom, in which most of cases had drowsiness 28cases (32.18%), amnesia 20 cases (22.98%),and sleepness 13cases(14.94%).

Table (5): Distribution of study cases according to post-ictal state symptom.

Symptom	No.	(%)
Drowsiness	28	32.18
Amnasia	20	22.98
Sleepness	13	14.94
Vomiting	10	11.49
Headache	8	9.19
Hallucination	4	4.59
Comatos	4	4.59

Table (6) shows the distribution of study cases according to EEG report, from 22 patients had EEG record, 14 cases (63.62%) were diagnosed as having seizure and 8 cases (36.36) were normal, 7cases (31.81%) had generalized seizure.

Table (6): Distribution of study cases according to EEG report.

EEG	No.	(%)
Normal	8	36.36
Generalized	7	31.81
Infantile spasm	3	13.63
Atypical	2	9.09
Absence	2	9.09
Total	**22**	**100**

Table (7) shows the distribution of study cases according to C.T. Scan report, where a19 patients were had C.T scan examination .

Table (7): Distribution of study cases according to C.T. Scan report

C.T. Scan	No.	(%)
Normal	9	47.36
Atrophy of brain	5	26.31
Dilated ventricle of brain	2	10.52
Peri-ventricular leukomalascia	2	10.52
Dandy-walker cyst	1	5.26
Total	19	100

Table (8) shows the distribution of study cases according to risk factor for seizure. Of total 40 patients, most of cases had no risk factor for seizure 24cases(60%) .

Table (8): Distribution of study cases according to risk factor for seizure

Risk factor	Cases	
	No.	(%)
+ve family history of seizure	**4**	**10**
Infection	**3**	**7.5**
Hypoxia	**2**	**5**
Metabolic condition	**2**	**5**
Systemic disorder	**1**	**2.5**
Head trauma	**2**	**5**
Toxins	**1**	**2.5**
Tumour	**1**	**2.5**
No risk factor	**24**	**60**
Total	**40**	**100**

Table (9) shows the distribution of study cases and control cases of serum iron in regarded to sex .

Table (9): Distribution of study cases and control cases of serum iron in regarded to sex

Serum Iron	Cases						Control					
	male	%	female	%	No.	%	male	%	female	%	No.	%
Normal	12	50	4	25	16	40	14	46.66	4	40	18	45
low	10	41.66	12	75	22	55	12	40	5	50	17	42.5
High	2	8.34	0	0	2	5	4	13.34	1	10	5	12.5
Total	24	100	16	100	40	100	30	100	10	100	40	40

Table (10) shows the distribution of study cases and control according to serum iron in regarded to age, Regarding study cases, most of cases were between ≥1 yr-<5 yrs.19 cases(47.5%) and also in control groups were between ≥1 yr-<5 yrs.21cases (52.5%).

Table (10): Distribution of study cases and control of serum iron according to age

Age	Cases					Control				
	No.	normal	low	high	%	No.	normal	low	high	%
≥ 4 mon.-<1 yr.	12	4	8	0	30	11	8	3	0	27.5
≥1 yr-<5 yrs.	19	7	12	0	47.5	21	8	12	1	52.5
≥5 yrs.-<10 yrs.	4	3	1	0	10	2	1	0	1	5
≥10 yrs.	5	2	1	2	12.5	6	1	2	3	15
Total	40	16	22	2	100	40	18	17	5	100

Table (11) shows the distribution of study cases and control according to serum iron in regarded to type of feeding, in study cases, mixed feeding groups16cases(40%), 10cases had low serum iron ,

Table (11): Distribution of study cases and control according to serum iron in regarded to type of feeding

Feeding	Cases					Control				
	No.	normal	low	high	%	No.	normal	low	high	%
Mixed	16	5	10	1	40	18	7	8	3	45
Bottle	13	5	8	0	32.5	14	7	6	1	35
Breast	11	6	4	1	27.5	8	4	3	1	20
Total	40	16	22	2	100	40	18	17	5	100

Table (12) shows the distribution of study cases and control of serum iron in regarded to residence, in study cases, most of them were rural area 27cases(67.5%), 15cases were low iron.

Table (12): Distribution of study cases and control of serum iron according to residence

Residence	Cases					Control				
	No.	normal	low	high	%	No.	normal	low	high	%
Rural	27	11	15	1	67.5	22	9	10	3	55
Urban	13	5	7	1	32.5	18	9	7	2	45
Total	40	16	22	2	100	40	18	17	5	100

Table (13) shows the distribution of study cases and control according to level of serum iron, in regarded to 40 cases of patients were taken, 22cases(55%) of them were of low iron .

Table (4.13): Distribution of study cases and control according to level of serum iron.

Serum Iron	Cases		Control	
	No.	(%)	No.	(%)
Normal	16	40	18	45
low	22	55	17	42.5
High	2	5	5	12.5
Total	40	100	40	100

P. value= 0.359805 (not significant) P. value> 0.05

Table (14)shows the distribution of study cases according to level of serum iron in regarded to seizure control, of total 40 cases of seizure.

Table (14): Distribution of study cases according to level of serum iron in regarded to seizure control

serum iron	Cases				Summation	
	Control		Uncontrolled		No.	(%)
	No.	(%)	No.	(%)		
Normal	5	12.5	11	27.5	16	40
low	7	17.5	15	37.5	22	55
High	1	2.5	1	2.5	2	5
Total	13	32.5	27	67.5	40	100

Discussion

Seizure paroxysmal disorders of the nervous system produce sudden, reversible changes in mental status or somatosensery function that tend to be stereotyped and repetitive in nature(1).

Most of our patient had pallor, this is goes with Baggett H C, Parkinson A J, Muth PT studies(11), which show that pallor constitute 60% in patients with seizure, this may be due to that most of our study can had iron deficiency which may present as pallor. Anemia resulting from lack of sufficient iron for synthesis of hemoglobin is the most common hematologic disease of infancy and childhood. It is estimated that 30% of the global population suffers from iron-deficiency anemia; most of those affecting life in developing countries (11). According to this study 22 patient only did EEG report , most of them have abnormal EEG(generalized seizure activity),this is goes with other study by Deonna T:study (12). This is that most of our cases were of generalized tonic clonic seizure.

The investigation of a seizure depends on many factors, including the age of the patient, the type and frequency of the seizure, and the presence or absence of neurologic findings and constitutional symptoms. Demonstration of paroxysmal discharges on the EEG during a clinical seizure is diagnostic of epilepsy, but seizures rarely occur acutely in the EEG laboratory. A normal EEG does not preclude the diagnosis of epilepsy, because the interictal recording is normal in 40 % of patients (12).

According to this study, most of the patients had no risk factors and the remaining had some risk factors, the most of which was positive

family history of seizure, this may be due to that seizure may have some genetic predilection, this study goes with Freeeman JM, Vinning EPG, Pillas DJ studies(13), which shows an increasing number of seizure have been identified that are the result of a genetic abnormality. To date, the chromosomal loci have been identified for seven epilepsy genes and three epilepsy syndromes, including benign familial neonatal convulsions (chromosomes 20q and 8q), fatal progressive myoclonic epilepsy or Unverricht-Lundborg disease (chromosome 21q), and juvenile myoclonic epilepsy (chromosome 6p). The gene locus on chromosome 6 also may be responsible for other types of generalize tonic-clonic seizures. Studies of large numbers of families that have other well-defined epilepsy syndromes likely will uncover additional epilepsy genes(13).

Despite the advent of molecular diagnosis and new neuroimaging techniques, the risk factor of most seizures in children remains unknown. The acute onset of seizures may result from cerebral trauma (head injury), CNS infection (meningitis, encephalitis), cerebrovascular diseases (infarction, arteriovenous malformation, hemorrhage, venous thrombosis), toxins (lead), brain tumor (cerebral or extracerebral), genetic/heredi-tary diseases (eg, Down syndrome, tuberous sclerosis), metabolic and systemic diseases (endocrine, renal), degenerative disorders (leukodystrophy) , or hereditary malformations(13).

In this study, most of patients with low serum iron having difficult to control seizure. In comparison those patients who had normal serum iron had good control of seizure, the association between iron deficiency (ID) and impaired neurocognitive function including delayed milestones of seizure is well-established, the association between (ID) and febrile seizures has been described in the last decade, Infants and toddlers, who are undergoing critical neurocognitive development, may be at particular risk for such More than 50% of patients had low serum iron, while among control groups aless no. of cases had low iron level, there was no significant difference in serum iron level indices between the two group.

ID was more prevalent among the cases with febrile convulsion, as compared to the controls, observed a significantly lower plasma iron in the first febrile convulsion group than in the reference group (49 of 75 vs.24 of 75), and Lazoff (7) reported a significantly higher rate of ID among children with febrile convulsions than in controls (15% vs. 9% and 30% vs.

12%, respectively), whereas, in contrast, other studies (8,9) reported that iron deficiency raises the threshold for seizures, this may be due to difference in sample size.

Conclusion: Most of cases that were taken had low serum iron 22cases (55%), although no significant result.The higher number of uncontrolled seizure had low serum iron, 15cases (37.5%).

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