LOW IRON STATUS: A POSSIBLE RISK FACTOR FOR FIRST FEBRILE SEIZURE

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CERTIFICATE

CERTIFICATE

Certified that this dissertation entitled **"LOW IRON STATUS: A POSSIBLE RISK FACTOR FOR FIRST FEBRILE SEIZURE"** is a bonafide work done by **Dr. B.R. SASIKUMAR.,** Post Graduate Student of Pediatric Medicine, Coimbatore Medical College & Hospital, Coimbatore- 641018, during the academic year 2009 - 2011.

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DECLARATION

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I declare that this dissertation entitled **"LOW IRON STATUS: A POSSIBLE RISK FACTOR FOR FIRST FEBRILE SEIZURE"** has been conducted by me at the Coimbatore Medical College Hospital, under the guidance and supervision of my Chief **Prof. Dr. K NEELAKANDAN, MD., DCH.,.** It is submitted in part of fulfillment of the award of the degree of M.D (Pediatrics) for the APRIL 2011 examination to be held under The Tamil Nadu Dr. M. G. R Medical University, Chennai. This has not been submitted previously by me for the award of any degree or diploma from any other university.

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INTRODUCTION

I. INTRODUCTION

SEIZURES IN CHILDHOOD

A seizure or convulsion is a paroxysmal, time-limited change in motor activity and/or behavior that result from abnormal electrical activity in the brain. Seizures are common in the pediatric age group and occur in approximately 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. Other events, such as breath-holding spells and gastro esophageal reflux, can cause events that simulate seizures. A few children also exhibit psychogenic seizures of psychiatric origin. Less than one third of seizures in children are caused by epilepsy, a condition in which seizures are triggered recurrently from within the brain.

For epidemiological classification purposes, epilepsy is considered to be present when two or more unprovoked seizures occur at an interval greater than 24 hr apart. The cumulative lifetime incidence of epilepsy is 3% and more than half of cases begin in childhood. However, the annual prevalence of epilepsy is lower (0.5—0.8%) because many children outgrow epilepsy.

Although the outlook for most children with symptomatic seizures or those associated with epilepsy is generally good, the seizures may signal a potentially serious underlying systemic or central nervous system (CNS) disorder that requires thorough investigation and management. For children with epilepsy, the prognosis is generally good, but 10—20% have persistent seizures refractory to drugs and those cases pose a diagnostic and management challenge.

Seizures have been recognized since ancient times and although improvement has been made in management over this century compared to the previous 2000 years, there are still far too many children whose lives are crippled by poorly controlled seizures.

Infants and children are more prone to have seizures than adults. This appears to reflect greater neuronal excitability at certain ages as the excitatory glutamate system and inhibitory gamma amino benzoic acid (GABA) system do not always balance each other. This also results in the tendency to exhibit symptomatic seizures related to high fever, virus infection, minor asphyxia, medication, bacterial toxins and biochemical upsets such as hypo- or hyper natremia and hypocalcemia

Childhood seizure differs from adult seizure since the brain is a developing organ. The clinical picture is not static and the pattern of fits may change with age, e.g. infantile spasms can evolve into Lennox—Gastaut syndrome. In addition, many types of seizures are restricted to childhood.

TERMINOLOGY

1. **A fit.** This is the clinical manifestation of a cerebral dysrhythmia, which may be convulsive, as in generalized tonic or tonic-clonic convulsions, or non convulsive as in absence seizures or complex partial seizures.

2. **A seizure**. A seizure describes a paroxysmal alteration in behavior due to any transient brain pathology. It includes cerebral dysrhythmias, transient ischemic or anoxic attacks, the latter being referred to as ‘faints’, and a miscellaneous group of paroxysmal brain abnormalities usually grouped as ‘funny turns’. The commonest examples of faints are reflex anoxic seizures (cyanotic breath-holding attacks) and reflex asystole seizures (pallid syncopal attack). The ischemic episodes of migraine would also be included in this group.

3. **A convulsion**. ‘All that convulses is not epilepsy.’ A convulsion is the term usually used when a child shows a sudden episode of decerebrate posturing, which is followed by clonic jerking. The clonic phase is often intermittent decerebrate posturing rather than a rhythmic clonic jerking. Loss of control by the cerebral cortex over the brainstem reticular formation from any cause will cause release of extensor decerebrate rigidity.

A convulsion may be due to cerebral dysrhythmia, as a true grand mal convulsion (in reality an episode of electrical decerebration) or a transient ischemic attack (acute anoxic rigidity), raised intracranial pressure with tentorial herniation or a toxic state (e.g. from drugs such as metoclopramide or haloperidol).

4. **An Epilepsy**. Epilepsy is recurrent fits due to repeated primary cerebral dysrhythmias.

MECHANISM OF SEIZURES

Although precise mechanisms of seizures are unknown, several physiologic factors are responsible for the development of a seizure. To initiate a seizure, there must be a group of neurons that are capable of generating a significant burst discharge and a GABAnergic inhibitory system. Seizure discharge transmission ultimately depends on excitatory glutamatergic synapses. Evidence suggests that excitatory amino acid neurotransmitters (glutamate, aspartate) may have a role in producing neuronal excitation by acting on specific cell receptors.

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. For example, lesions in the temporal lobe (including slow-growing gliomas, hamartomas, gliosis, and arteriovenous malformations) cause seizures, and when the abnormal tissue is removed

surgically, the seizures are likely to cease. Further, convulsions may be produced in experimental animals by the phenomenon of kindling. In this repeated subconvulsive stimulation of the brain (e.g., amygdala) ultimately leads to a generalized convulsion. Kindling may be responsible for the development of epilepsy in humans after an injury to the brain. In humans, it has been proposed that recurrent seizure activity from an abnormal temporal lobe may produce seizures in the contra lateral normal temporal lobe by transmission of the stimulus via the corpus callosum.

Seizures are more common in infants and in immature experimental animals. Certain seizures in the pediatric population are age specific (e.g., infantile spasms); this observation suggests that the underdeveloped brain is more susceptible to specific seizures than is the brain of an older child or adult. Genetic factors account for at least 20% of all cases of epilepsy. Using linkage analyses, the chromosomal location of several familial epilepsies has been identified, including benign neonatal convulsions (20q and 8q), juvenile myoclonic epilepsy (6p), and progressive myoclonic epilepsy (21q22.3). The genetic defect of benign familial neonatal convulsions has been characterized by the identification of submicroscopic deletion of chromosome 20q 13.3. Furthermore, the substantia nigra has an integral role in the development of generalized seizures. Electrographic seizure activity spreads within the substantia nigra, causing an increase in uptake of 2-deoxyglucose in adult animals, but there is little or no metabolic activity within the substantia nigra when immature animals have a convulsion. It has been proposed

that the functional immaturity of the substantia nigra may have a role in the increased seizure susceptibility of the immature brain. Additionally, the ‘G-aminobutyric acid (GABA) -sensitive substantia nigra pars reticulata neurons play a part in preventing seizures. It is likely that substantia nigra outflow tracts modulate and regulate seizure.

FEBRILE SEIZURES

Almost three decades ago, Livingston (1) observed that children with febrile seizures fared considerably better than children with epileptic convulsions not activated by fever; their prognosis with respect to epilepsy was uniformly more favorable, and they were more likely to be neurologically normal. Febrile seizures are now recognized to be a relatively benign, age-dependent epilepsy syndrome and the most prevalent form of seizure in early life.

The National Institutes of Health (NIH) Consensus Development Conference on the Management of Febrile Seizures defined a febrile seizure as “an event in infancy or childhood, usually occurring between 6 months and 5 years of age, associated with fever but without evidence of intracranial infection or defined cause” (2). This definition is useful because it emphasizes age specificity and the absence of underlying brain abnormalities. It also implies that febrile seizures are not true epilepsy because affected individuals are not predisposed to recurrent afebrile episodes.

In clinical practice, however, the NIH definition must be interpreted with caution. Intracranial infection may not be readily apparent, especially in very young infants. Although few advocate extensive testing in a healthy child with a brief nonfocal febrile seizure, an infant or child in febrile hemiconvulsive status epilepticus requires immediate medical attention.

Familiarity with the clinical manifestations and long- term prognosis of febrile seizures is essential in caring for affected individuals. Epidemiologic studies have been especially useful in identifying features of the seizure or the patient that involve adverse consequences. Understanding these factors forms the basis of proper seizure management and family counseling.

PREDISPOSING FACTORS

Genetics:

No consensus has been reached on the mode of inheritance of febrile seizures or their clinical expression. Autosomal dominant autosomal recessive and polygenic theories have all been formulated.

Regardless of the clinical semiology, febrile seizures are approximately two to three times more common among family members of affected children than in the general population (3). Affected parents increase the risk of febrile seizures in siblings. The risk raise when both parents are affected and increases further in proportion to the number of febrile seizures experienced by the proband. A higher incidence of afebrile epilepsy has been found in first-degree relatives of febrile seizure patients. Conversely, the occurrence of febrile seizures in first-degree relatives is itself a risk factor for febrile seizure recurrence. Siblings have the greatest risk, followed by offspring, nieces, and nephews. Coexistence of febrile seizures and epilepsy increases the risk of both disorders in siblings (4).

The incidence of febrile seizures also varies according to geographic region and race. Parents and siblings of Asian children are at considerably greater risk for febrile seizures than are Western families. Sibling risk approaches 30% if one parent has had a febrile seizure. The difference in frequency of febrile seizures in Asian compared with European or North American families suggests a strong, genetically

determined population effect. Linkage studies in several large families have mapped the febrile seizure gene to chromosomes 19p and 8q13-21.

Age:

The onset of febrile seizures generally follows a bell- shaped pattern. Ninety four percent occur within the first 3 years of life and 6% after 3 years of age. Approximately one half appears during the second year of life, with a peak incidence between 18 and 24 months.

Febrile seizures occurring before 6 months of age should always raise the suspicion of infectious causes; bacterial meningitis must be excluded by lumbar puncture. Febrile seizures after 5 years of age should be managed cautiously, because benign causes are less common in older children.

Fever:

Febrile seizures typically occur relatively early in an infectious illness, usually during the raise phase of the temperature curve. Rectal temperatures at this time may exceed 39.2^{o}C, and approximately one fourth of seizures occur at a temperature above 40.2^{o}C. Despite the implicit relationship between fever and seizure activation, temperature itself probably does not lower the seizure threshold. The incidence of febrile seizures does not increase in proportion to temperature elevation, and febrile seizures are uncommon in the later stages of persistent illness. Moreover, children between the ages of 16 and 18 months who

experience fever greater than 40^{o}C have sevenfold reduction in seizure recurrence compared with children with fever below 40^{o}C (5). A brief duration of fever before the initial febrile seizure has been linked to an increased risk of seizure recurrence.

Febrile seizures typically are associated with common childhood infections, most frequently upper respiratory tract, middle ear, and gastrointestinal, that are viral. Bacterial infections including bacteremia, pneumonia, sepsis, and meningitis, are rare concomitants of febrile seizures. None of the common childhood infectious illnesses, viral or bacterial, appears uniquely capable of activating febrile seizures.

Febrile seizures in conjunction with shigellosis constitute the most frequent extraintestinal manifestations of this infection. A direct neurotoxic effect of the shigella bacterium on seizure threshold has been proposed.

Immunization-related seizures also manifest with fever, usually within 48 hours of inoculation. Approximately one fourth are related to administration of diphtheria-pertusis-tetanus (DPT) vaccine, and one fourth follows measles immunization. Data from the National Collaborative Perinatal Project indicate that age of onset, personal and family histories, and clinical presentations of postimmunization seizures resemble those of febrile seizures from infectious causes.

SIMPLE FEBRILE CONVULSIONS

Simple febrile convulsions are solitary events lasting less than 15 minutes and lacking focality. They occur in neurologically normal children and are not associated with persistent deficits. The source of the fever is always outside the central nervous system.

Between 80% and 90% of all febrile seizures are simple episode. Despite their common occurrence, the sporadic nature and brief duration of febrile seizures make analysis difficult. Febrile seizures are described as tonic, clonic, or tonic-clonic events that usually begin without warning and display upward eye deviation, as consciousness is lost. Atonic forms are rare, and postictal depression is generally brief.

Electroencephalography (EEG) has not been particularly useful in the evaluation of simple febrile seizures. Although paroxysmal and non-specific EEG abnormalities are often evident within 24 hours of seizure onset, they have little prognostic significance. Slow-wave activity occurs in up to one third of patients and is often bilateral and prominent in the posterior regions. Twenty percent of patients, usually older than 2.5 years, have generalized spike-and-wave discharges on EEG.

In a longitudinal study of 89 febrile seizure patients followed until puberty, Doose et al. identified three patterns of EEG abnormality: rhythms of 4 to 7 Hz, generalized spike-and-wave discharges, and photosensitivity (6). None were specific for febrile seizures because all

had been described in generalized epilepsies as well. Genetic factors probably account for the age-related expression of these EEG patterns in benign simple febrile seizures.

The evaluation of simple febrile seizures should rely primarily on careful history taking. This approach, especially important in children who are normal, "children who have their first febrile convulsion need no more tests than the clinical findings dictate." An exception is the requirement for lumbar puncture in all patients under 6 months old who lack any of the classic signs of bacterial meningitis. The rule that all children younger than 18 months of age with a first febrile seizure should always undergo lumbar puncture is probably excessive, and each child should be evaluated individually. When meningitis is suspected clinically, lumbar puncture should be performed promptly.

Hospitalization is rarely needed after a simple febrile seizure. Testing can usually be performed in an outpatient setting because risk of seizure recurrence is low, Even then, pediatricians may hospitalize patients who can be sent home safely.

COMPLEX FEBRILE SEIZURES

The concept of a "complex" febrile seizure originated with epidemiological studies indicating that several patient and seizure-related variables predicted higher rates of subsequent epilepsy: seizure duration longer than 15 minutes, focal seizure manifestations, seizure recurrence

within 24 hours, abnormal neurological status, and afebrile seizures in a parent or sibling. Six percent of patients with two or more risk factors developed afebrile epilepsy by the age of 7 years, compared with only 0.9% if risk factors were absent (7).

Anneqers et al. reveal a less favorable prognosis for complex febrile seizures (8). Seventeen percent of neurologically impaired children with complex febrile seizure manifestations developed epilepsy by the third decade, compared with 2.5% of children who lacked risk factors. The occurrence of focal, recurrent, and prolonged seizures raised the risk of afebrile episodes to nearly 50%.

Children with complex febrile convulsions may subsequently exhibit a variety of febrile seizure patterns. The National Collaborative Perinatal Project found generalized tonic-clonic seizures to be most frequent and absence or myoclonic seizures less common. 29 cases of afebrile epilepsy developed in a cohort of 666 patients with febrile seizures. Seizures were classified as focal in 16 cases and of temporal origin in 10 cases. Generalized tonic-clonic seizures were reported in 12 patients, three of whom also had absence seizures. One patient had unclassifiable seizures. In a retrospective analysis of 504 children with epilepsy, Camfield et al. found a 14.9% incidence of preceding febrile seizures (9). Febrile seizures most often preceded generalized tonic-clonic afebrile seizures and were regarded as fundamentally indicative of reduced seizure threshold.

Complex febrile seizures must be managed more aggressively than simple episodes. Meningitis must be excluded by timely performance of lumbar puncture, and neuroimaging studies are indicated to detect structural lesions. In acute bacterial meningitis, focal febrile seizures may accompany cortical vein or sagittal sinus thrombosis.

Although children with complex febrile seizures may be expected to show a higher rate of abnormal EEG recordings than normal, confirmatory data are sparse. Studies of febrile seizures rarely include EEG findings, although this type of information would enhance the value of EEG in the management of febrile seizures.

FEBRILE STATUS EPILEPTICUS

Although most febrile seizures are self-limited, prolonged episodes and febrile status epilepticus are not rare. The reported occurrence of epilepsy, brain damage, or death after febrile status epilepticus further underscores its serious nature. Of 1706 children with febrile seizures followed in the National Collaborative Perinatal Project, 8% experienced seizures longer than 15 minutes, and 4% had seizures longer than 30 minutes. Febrile status epilepticus accounted for approximately one fourth of all cases of status epilepticus in children and is often the initial presentation of chronic epilepsy.

Children with febrile status epilepticus are usually mentally and physically normal. As in simple febrile seizures, common childhood

infectious diseases and immunizations are the primary cause of the fever. An association between female sex and febrile status epilepticus has been observed and younger age strongly predisposes to prolonged unilateral febrile seizures (10).

Postmortem studies of patients dying in febrile status epilepticus reveal widespread neuronal necrosis of the cortex, basal ganglia, thalamus, cerebellum, and porolimbic structures. Rare inflammatory changes suggest that seizures and anoxia, rather than infection, are the primary causes of mortality.

Prospective studies reveal that the risk of death or permanent neurological impairment after febrile status epilepticus is negligible. The tendency for febrile status epilepticus to recur is especially low in neurologically normal children, and mortality in this group has markedly declined. None of the 1,706 patients reported by the National Collaborative Perinatal Project died as a consequence of febrile seizures.

A few infants present with severe febrile hemiconvulsive status that is followed by permanent hemiplegia. After a variable seizure-free interval, they develop chronic focal epilepsy that can persist for many years. This presentation, called the hemiconvulsion-hemiplegia epilepsy (HHE) syndrome, was described by Gastaut et al. (11), who regarded it as distinct from other prenatal or perinatal causes of infantile hemiplegia and epilepsy.

RECURRENCE OF FEBRILE SEIZURES

Approximately one third of patients with febrile seizures experience further attacks; of this group, one half will have a third seizure and only 9% suffer three or more attacks.

Age of onset is the most important predictor of febrile seizure recurrence. One half of the infants younger than 1 year of age at the time of their first febrile seizure will have a recurrence, compared with 20% of children older than 3 years. Young age at onset, a history of febrile seizures in first-degree relatives, low-grade fever in the emergency department, and brief interval between fever onset and seizure presentation are strong independent predictors of febrile seizure recurrence (13). Recurrences generally occur within 1 year but are no more likely in children who had a complex febrile seizure than in those who had a simple febrile seizure.

Approximately one half of all recurrent febrile seizures occur within the 2 hours after onset of fever in a subsequent febrile episode. Young age at onset and high temperature favor recurrence.

FEBRILE SEIZURES AND LATER EPILEPSY

Between 1.5% and 4.6% of children with febrile seizures develop later afebrile seizures. Although this rate is significantly higher than in the general population, it reflects primarily infants and children who had one or more complex febrile seizure.

The mechanism by which febrile seizures predispose to later epilepsy is much less clear. Prolonged febrile convulsions in early infancy may precede a variety of seizures but are particularly common in children who develop intractable seizures of temporal lobe origin. Histopathologic studies of temporal lobectomy specimens demonstrate hippocampal sclerosis in approximately one half of the cases. This lesion has been hypothesized to result from the asphyxia that typically accompanies prolonged febrile seizures, especially febrile status epilepticus. Prolonged febrile seizures in childhood are known to have adverse physiologic consequences, including increased cerebral metabolic demand and systemic changes including hypoxia, hypoglycemia, and arterial hypotension. Hyperpyrexia can increase cerebral metabolic rate by as much as 25%.

The clinical and experimental sequelae of prolonged febrile seizures are difficult to reconcile with epidemiological data indicating that most severe attacks do not produce long-lasting consequences. Febrile seizures should therefore be considered to represent a continuum of brain dysfunction ranging from very mild local cellular changes to severe generalized damage or hemiatrophy.

Neuroimaging studies further support the concept of selective hippocampal vulnerability to prolonged or recurrent febrile seizures in susceptible individuals. Signs of preexisting hippocampal abnormalities and electrographic seizure discharges in the temporal lobe in several

infants suggest primary febrile seizure onset in the temporal lobe. Hippocampal volumetry reveals smaller total volumes and a larger right-to-left ratio in children with complex febrile seizures. Increasing duration of the seizure is inversely associated with ipsilateral, but not contralateral, hippocampal volume, suggesting that the deleterious effects of persistent seizures remain localized to the epileptogenic zone.

A complex relationship exists among age, sex, and hemispheric vulnerability in children who develop temporal lobe seizures after prolonged febrile convulsions. Left-sided hippocampal sclerosis is more common after prolonged febrile seizures in the first year of life but is rare after 2 years of age, whereas right-sided hippocampal sclerosis is equally prevalent throughout the first 4 years of life. The risk for hippocampal sclerosis in both sexes is highest in the first year of life but declines gradually in boys and precipitously in girls. These observations suggest differential rates of vulnerability for each cerebral hemisphere in both sexes.

GENETIC INFLUENCES

Genetic factors appear to play a role when epilepsy develops after febrile seizures. Temporal lobe seizures are more likely to begin early but remit permanently if a first degree relative had a febrile seizure . A single gene is held responsible, because the siblings of patients with temporal lobe and febrile seizures have a similar incidence of febrile seizures alone.

The inherited syndrome of generalized epilepsy with febrile seizures plus (GEFS+) has been described in a large kindred from rural Victoria, Australia. The most common clinical phenotype includes children with febrile seizures in early childhood who develop persistent febrile seizures beyond age 6 years. Other affected individuals have a variety of afebrile seizures. Seizures typically cease by mid-adolescence.

This pattern of inheritance is consistent with an autosomial dominant mode, and linkage studies map GEFS+ to chromosome 2q. Another autosomal dominant febrile seizure locus has been identified on chromosome 19p.

Collectively, children with complex febrile seizures can be said to have a small but identifiable risk for later epilepsy, based on genetic, developmental, and acquired factors. If these children develop persistent temporal lobe seizures, they are likely to continue to experience seizures in later life.

FEBRILE SEIZURES AND NEUROPSYCHOLOGICAL STATUS

The consequences of febrile seizures on later intellectual functioning and behavior have been studied extensively. Although some children with febrile seizures had later cognitive sequalae, virtually all had neurologic deficits predating their convulsions.

Two large longitudinal, population-based studies provide strong evidence that febrile seizures do not adversely affect neuropsychological

status. Ellenberg and Nelson (13) studied intellectual and academic function after febrile seizures in 431 sibling pairs 7 years of age who were part of the National Collaborative Perinatal Project. Children with febrile seizures and normal intelligence achieved reading and spelling milestones at rates similar to those of their seizure-free siblings. Poor academic performance on the Wide Range Achievement Test was equally frequent in febrile seizure patients and sibling controls. The National Child Development Study, completed in the United Kingdom, also found that children with febrile seizures did not differ from controls in behavior, height, head circumference, or academic achievement.

INVESTIGATIONS

The main differential diagnosis is meningitis, non-accidental injury or metabolic disease. The history and examination may suggest an obvious source of the fever such as an otitis media or pharyngitis but this should not prevent a high index of suspicion for more serious infection, e.g. pneumococcal meningitis. Up to 25% of cases of pneumococcal meningitis may present with a fit, pyrexia and an otitis media. Under the age of 6 months a convulsion associated with fever should be considered as a sign of CNS infection and cerebrospinal fluid (CSF) examination mandatory. Beyond that age if any doubt exists about the possibility of meningitis, a lumbar puncture with the examination of the CSF is indicated.

If the child has not recovered consciousness on arrival in hospital the assessment is more difficult. If he has been given diazepam or phenobarbitone prior to admission then this may be the reason. Detailed examination needs to be performed looking for signs of raised intracranial pressure or focal neurological abnormality. If these are present then the management should be as for an acute encephalopathy with raised ICP and imaging must precede lumbar puncture. Seizure induced CSF abnormalities are rare in children and all patients with abnormal CSF after a seizure should be thoroughly evaluated for other causes. The possibility of viral meningoencephalitis should also be kept in mind, especially that caused by Herpes simplex.

EEG (Electroencephalogram)

An EEG carried out in the week after a febrile convulsion will be abnormal in a third of cases, showing posterior slow wave activity which may be bilateral or unilateral. Such abnormalities are not helpful for the prediction of subsequent epilepsy. The EEG at a later age, e.g. 5 years, often shows abnormality such as spike and wave activity which indicates a genetic predisposition but not that the child has epilepsy. An EEG is not warranted after a simple febrile seizure but may be useful for evaluating patients with an atypical feature or with other risk factors for later epilepsy. Similarly neuroimaging is also not useful for children with simple febrile convulsions but may be considered for children with atypical features.

PROGNOSIS

Excellent; less than 3% develop long-term epilepsy despite the strong genetic predisposition, but the prognosis is more guarded if the convulsion is prolonged or atypical. Up to 40% may have another convulsion and 15% a third episode. If the child suffers from multiple repeated febrile convulsions the possibility of early malignant epilepsy such as myoclonic epilepsy of Dravet exists.

Subsequent epilepsy is more likely if:

• the child is less than 12 months old;

• a complex initial convulsion occurred with neurological signs;

• febrile convulsions are present in first-degree relatives;

• prolonged fits lasting more than 30 minute;

• there are more than three episodes.

If two or more risk factors are present, the risk of subsequent epilepsy rises to 10%. The basis of the subsequent epilepsy is thought in many cases to be due to brain damage to the temporal lobes acquired during a prolonged or complicated seizure rather than due to the genetic low threshold.

MANAGEMENT

Recurrences of febrile convulsions can be prevented by medication. The main reason for preventing recurrences would be to avoid a prolonged seizure. Most prolonged febrile seizures are first seizures and the risk for recurrence of a long seizure is low (1—4%).

Prolonged seizures can he prevented by the parents giving rectal diazepam when the seizure has lasted 5 min. In most cases prophylactic medication will not be required. Prophylactic oral medication may be used instead of rectal diazepam but prophylaxis does not give a guarantee that recurrence will not happen.

Continuous prophylaxis.

Both phenobarbitone and sodium valproate have been shown to significantly reduce the rate of recurrences when taken continuously. Anticonvulsants, which act on the voltage-gated sodium ionophore, such as phenytoin and carbamazepine, are not effective prophylaxis. Recurrence rates with effective drugs are around 8—12% compared with 30% for controls. Phenobarbitone has fallen into disfavor because of the high incidence (30—50%) of behavioral side effects in the form of hyperactive and aggressive behavior. Other problems are the possibility of seizures if the drug is discontinued suddenly by the parent, the possibility of acute poisoning in a child or siblings and concerns about the effect on learning in young children.

For this reason sodium valproate has become the most widely used drug for continuous prophylaxis. It does not have any obvious effects on learning and is usually well tolerated although there have been reports of rare fatal hepatic toxicity. The risk of hepatotoxicity in the under-3 population is 1 in 500 whereas the incidence in adults is 1 in 30 000. Prolonged anti-convulsant prophylaxis for preventing recurrent febrile seizures is no longer recommended. Those children whose risk of recurrence is high should probably be started on continuous prophylaxis after the first febrile convulsion.

INTERMITTENT PROPHYLAXIS

The rationale for this method is that oral diazepam given at the start of the febrile illness will prevent convulsions occurring. This has been shown to reduce recurrence rates from 27% to 12% of cases. At the onset of each febrile illness oral diazepam 0.3mg/kg 8^{th} hourly is administered for the duration of the illness (usually 2-3 days). The side effects are usually minor, but adjusting the dose may reduce symptoms of lethargy, irritability and ataxia. The strategy may be useful when parental anxiety associated with febrile seizure is severe.

IRON DEFICIENCY

Anemia resulting from lack of sufficient iron for synthesis of hemoglobin is the most common hematologic disease of infancy and childhood. Its frequency is related to certain basic aspects of iron metabolism and nutrition. The body of a newborn infant contains about 0.5 g of iron whereas the adult content is estimated at 5 g. To make up for this discrepancy, an average of 0.8 mg of iron must be absorbed each day during the first 15 yr of life. In addition to this growth requirement, a small amount is necessary to balance normal losses of iron by shedding of cells. Accordingly, to maintain positive iron balance in childhood, about 1 mg of iron must be absorbed each day.

Iron is absorbed in the proximal small intestine, mediated in part by a variety of duodenal proteins. Because absorption of dietary iron is assumed to be about 10%, a diet containing 8-10 mg of iron daily is necessary for optimal nutrition.

Iron is absorbed two to three times more efficiently from human milk than from cow’s milk, perhaps partly because of differences in calcium content. Breast-fed infants may, therefore, require less iron from other foods. During the first years of life, because relatively small quantities of iron-rich foods are eaten, it is often difficult to attain sufficient iron. For this reason, the diet should include such foods as infant cereals or formulas that have been fortified with iron; both of these are very effective in preventing iron deficiency. Formulas with 7—12

mg/l for full-term infants and premature infant formulas with 15 mg/L for infants less than 1,800 g at birth are effective. Infants breast-fed exclusively should receive iron supplementation from 4 months of age. Should the diet become inadequate or external blood loss occur, anemia ensues rapidly.

ETIOLOGY

Low birth weight and unusual perinatal hemorrhage are associated with decreases in neonatal hemoglobin mass and stores of iron. As the high hemoglobin concentration of the newborn infant falls during the first 2—3 mo of life, considerable iron is reclaimed and stored. These reclaimed stores are usually sufficient for blood formation in the first 6—9 months of life in term infants. In low-birth weight infants or those with perinatal blood loss, stored iron may be depleted earlier and dietary sources become of paramount importance. In term infants, anemia caused solely by inadequate dietary iron is unusual before 6 month and usually occurs at 9—24 mo of age. Thereafter, it is relatively infrequent. The usual dietary pattern observed in infants with iron-deficiency is consumption of large amounts of cow's milk and of foods not supplemented with iron.

Blood loss must be considered a possible cause in every case of iron-deficiency anemia, particularly in older children. Chronic iron-deficiency anemia from occult bleeding may be caused by a lesion of the gastrointestinal tract, such as a peptic ulcer, Meckel's diverticulum,

polyp, or hemangioma, or by inflammatory bowel disease. In some geographic areas, hookworm infestation is an important cause of iron deficiency. Pulmonary hemosiderosis may be associated with unrecognized bleeding in the lungs and recurrent iron deficiency after treatment with iron. Chronic diarrhea in early childhood may be associated with considerable unrecognized blood loss. Some infants with severe iron deficiency have chronic intestinal blood loss induced by exposure to a heat-labile protein in whole cow's milk.

Loss of blood in the stools each day can be prevented either by reducing the quantity of whole cow's milk to 1 pint/24 hr or less, by using heated or evaporated milk, or by feeding a milk substitute. This gastrointestinal reaction is not related to enzymatic abnormalities in the mucosa, such as lacatase deficiency, or to typical "milk allergy." Involved infants characteristically develop anemia that is more severe and occurs earlier than would be expected simply from an inadequate intake of iron.

Histologic abnormalities of the mucosa of the gastrointestinal tract, such as blunting of the villi, are present in advanced iron deficiency anemia and may cause leakage of blood and decreased absorption of iron, further compounding the problem.

SPECTRUM OF IRON DEFICIENCY

Pallor is the most important sign of iron deficiency. In mild to moderate iron deficiency (hemoglobin levels of 6—10 g/dL), compensatory mechanisms, including increased levels of 2,3-diphosphoglycerate (2, 3-DPG) and a shift of the oxygen dissociation curve, may be so effective that few symptoms of anemia are noted, although affected children may be irritable.

Pagophagia, the desire to ingest unusual substances such as ice or dirt, may be present. In some children, ingestion of lead-containing substances may lead to concomitant plumbism. When the hemoglobin level falls below 5 g/dl, irritability and anorexia are prominent. Tachycardia and cardiac dilation occur, and systolic murmurs are often present.

Children with iron deficiency anemia may be obese or maybe underweight, with other evidence of poor nutrition. The irritability and anorexia characteristic of advanced cases may reflect deficiency in tissue iron, because with iron therapy striking improvement in behavior frequently occurs before significant hematological improvement is noted.

Iron deficiency may have effects on neurological and intellectual function. A number of reports suggest that iron-deficiency anemia, and even iron deficiency without significant anemia, affects attention span, alertness, and learning of both infants and adolescents. In a controlled

trial, adolescent girls with serum ferritin levels of 10 ng/ml or less but without anemia had improved verbal learning and memory after taking iron for 8wk.

In a double-blinded placebo controlled trail of iron treatment for breath-holding spells, more than 50% of the treatment group had no further breath-holding episodes and another 36.4% had partial response with 50 or fewer episodes. None of the placebo-controlled group had a complete response and fewer than 6% had a partial response. (14).

Iron deficiency although a common entity is rarely considered as a primary etiology in frequently observed pediatric neurological disorders.

There seems to be a flurry of studies recently relating iron deficiency to a variety of neurological problems. While the most obvious consequence of iron deficiency is anemia, at the cellular level, iron is involved in a variety of process and its deficiency virtually affects every organ system including the central nervous system. Iron and its role in the central and peripheral nervous system functioning has been investigated in animal models and in clinical human studies. Deficiency of iron in children has been implicated in developmental abnormalities, ischemic stroke, venous thrombosis, breath-holding spells and other neurological abnormalities. The most intriguing recent description relates to the association between febrile seizures and iron deficiency. Though the pathophysiology remains speculative iron is involved in the metabolism of several neurotransmitters. In addition monoamine oxidase and

aldehyde oxidase are decreased in iron deficiency, which has been correlated with the neurological abnormalities.

PATHOPHYSIOLOGY

Some of the clinical manifestations may be related to the role of iron in certain enzymatic reactions. Monoamine oxidase (MAO), an iron-dependent enzyme, has a crucial role in neurochemical reactions in the central nervous system. Iron deficiency produces decreases in the activities of enzymes such as catalase and cytochromes. Catalase and peroxidase contain iron, but their biologic essentiality is not well established. Iron deficiency alters the electron transport and neurotransmitter synthesis in the brain thereby affecting the normal function of the neural tissue (15, 16)

It is obvious that iron deficiency during gestation and lactation results in abnormalities in brain development in animal models that are irreversible. All this suggests that it is imperative to prevent iron deficiency in woman of childbearing age, including during gestation and also throughout infancy and childhood. Developmental problems, risk of pediatric stroke, the occurrence of febrile seizures and breath-holding spells are perhaps the tip of iceberg of the neurological consequences of iron deficiency. With appropriate recognition, treatment or better yet prevention, the neurological sequelae of iron deficiency are entirely preventable and perhaps reversible.

LITERATURE REVIEW

II. LITERATURE REVIEW

Daoud AS, et al in a case control study at King Hussian Medical College, Irbid, Jordan, studied the relation of iron status and first febrile seizure in a sample of 75 children. It was found that the mean ferritin level was significantly lower in cases (29.5+/- 21.3 ng/l) than in controls (53.3+/- 37.6ng/l) with P=. 0001. A higher proportion of cases with febrile seizures had low Hb. MCV and MCH than did the controls but the difference were not statistically significant (17).

Rehman N, et al in a case control study conducted at the the Aga Khan University Hospital, Karachi in 2001, studied the association between iron deficiency and febrile convulsions in a sample of 60 children. The mean age for febrile seizures was 22.97+/- 9.52 months. There was no significant difference in the gender distribution. Iron deficiency was significantly more among children with febrile seizures as compared to controls. Hb<11gm/dl (P=.000) Hct<30 (P=<.01) MCV<70fl (P=<.0) MCH<24pg(P=.001) and serum ferritin <10ng/ml (P<.000) (18).

Alfredo pisacan et al of Castellammare Di Stabie Hospital, Naples in their case control study about the association between iron deficiency and febrile seizures in a sample of 156 children, found that the mean age for febrile seizure was 15 months. There was no significant difference in gender distribution. Iron deficiency was significantly more common in febrile seizures group than in controls (19).

Amirsalari, et al studied the relationship between iron deficiency anemia and febrile seizures . This case - control study was published in Iranian journal of pediatrics 1/1/2010 performed on 132 cases and 88 controls, aged 9 months to 5 years, from July 2007 to June 2009 in Baqyiatallah Hospital. Patients were selected using simple random sampling. The case group included children with first febrile seizure (core temperature over 38.5˚C during seizure) without a central nervous system infection or an acute brain insult. The control group included children suffering from a febrile illness without seizure. Iron deficiency anemia was defined with one of these laboratory indexes: 1) Hemoglobin (Hb) <10.5mg/dl 2) Plasma ferritin <12ng/ml 3) Mean corpuscular volume (MCV) <70 fl. The data collected from patients were analyzed with SPSS.13 software. Low plasma ferritin was found in 35 cases (26.5%) compared to 26 controls (29.5%), low Hb level was found in 4 cases (3%) compared to 6 controls (6.8%) and low MCV was found in 5 cases (3.8%) compared to 6 controls (6.8%).There was no significant difference in plasma ferritin , Hb level and MCV indices between the two group. Conclusion Considering the above-mentioned results, there is no relationship between iron deficiency anemia and febrile seizures.

Rajwanti K Vaswani et al From Department of Pediatrics, in a case control study at King Edward Memorial Hospital, Parel, Mumbai, India, .studied the role of iron deficiency as a risk factor for first febrile seizure in children. Fifty children between 6 months to 6 years with first febrile seizure (Cases) and 50 children with febrile illness but without convulsions (Controls) were enrolled from the pediatric ward of a tertiary care hospital. Iron deficiency was determined by estimation of hemoglobin, red blood cell indices and serum ferritin. The mean serum ferritin level (ng/ml) was significantly low in Cases (31.9 ± 31.0) as compared to Controls (53.9 ± 56.5) with P = 0.003. Iron deficiency could be a potential risk factor for febrile seizure in children.this study was Published online: May 10, 2009. In Indian pediatrics.

Momen Ali Akbar et al in a case control study published in Iran Journal Child Neurology sept 2010 evaluated IRON STATUS IN 9-MONTH TO 5-YEAR-OLD CHILDREN WITH FEBRILE SEIZURES. They took Two sex and age matched groups (n=50 in each) of 9-month to 5-year-old febrile children who were admitted to Abuzar Hospital between September 2003 and October 2004. The first group, or the case group, included children with the first attack of febrile seizure and the second group, or the control group, included febrile children without

seizure. Blood samples were collected for measuring complete blood count (CBC) indices, serum Iron, ferritin and total iron binding capacity (TIBC) levels. There was no significant difference in CBC, Iron and TIBC between two groups but a significant difference was seen in MCV(Mean Corpuscular Volume), especially in females (P< 0.017). The ferritin level in the case group was significantly lower (30.3 ±16.5 ng /ml) than the control group (84.2 ±28.5 ng/ml) (P< 0.000). Findings of this study suggested a positive association between iron deficiency and the first febrile seizure in children.

Richard Idro et al studied Iron Deficiency and Acute Seizures in Children Living in Rural Kenya and did a Meta-Analysis. They examined the hypothesis that iron deficiency is associated with an increased risk of acute seizures in children in a malaria endemic area. They recruited 133 children, aged 3–156 months, who presented to a district hospital on the Kenyan coast with acute seizures and frequency-matched those to children of similar ages but without seizures. They defined iron deficiency according to the presence of malarial infection and evidence of inflammation. In patients with malaria, defined iron deficiency as plasma ferritin,30ng/ml if plasma C-reactive protein (CRP) was,50mg/ml or ferritin,273ng/ml if CRP$50mg/ml, and in those without malaria, as ferritin,12ng/ml if CRP,10mg/ml or ferritin,30ng/ml if CRP$10mg/ml.

published in English between January 1966 and December 2009 and available through PUBMED that have examined the relationship between iron deficiency and febrile seizures in children. Kenyan case control study, cases and controls were similar, except more cases reported past seizures. Malaria was associated with two-thirds of all seizures. Eighty one (30.5%) children had iron deficiency. Iron deficiency was neither associated with an increased risk of acute seizures (45/133[33.8%] cases were iron deficient compared to 36/133[27.1%] controls, p = 0.230) nor status epilepticus and it did not affect seizure semiology. Similar results were obtained when children with malaria, known to cause acute symptomatic seizures in addition to febrile seizures were excluded. However, in a meta-analysis that combined all eight case-control studies that have examined the association between iron deficiency and acute/febrile seizures to-date, iron deficiency, described in 310/1,018(30.5%) cases and in 230/1,049(21.9%) controls, was associated with a significantly increased risk of seizures, weighted OR 1.79(95%CI 1.03–3.09). They concluded that Iron deficiency is not associated with an increased risk of all acute seizures in children but of febrile seizures.

Dawn S. Hartfield et al published an article in clinical pediatrics Canada, studied The Association between iron deficiency and febrile seizures in a large cohort of children aged 6 to 36 months. A retrospective case control study with 361 patients who presented with febrile seizures to the emergency department and 390 otherwise healthy controls who presented with a febrile illness to the emergency department were reviewed to determine iron status using the MCV, RDW, and hemoglobin. A total of 9% of cases had iron deficiency (ID) and 6% had iron deficiency anemia (IDA), compared to 5% and 4% of controls respectively. The conditional logistic regression odds ratio for ID in patients with febrile seizures was 1.84 (95% CI, 1.02-3.31). They concluded that, children with febrile seizures were almost twice as likely to be iron deficient as those with febrile illness alone.

Kobrinsky Nl, et al in a case control study at University of North Dakota, Fargo studied the effect of iron status on the seizure threshold in a sample of 51 children. It has been found that the patients with febrile seizures were less frequently iron deficient than the control (20).

STUDY JUSTIFICATION

III. STUDY JUSTIFICATION

From the studies done at Naples(Alfredo pisacan et al)(19), Karachi(Rehman N,et al)(18), Jordan(Daoud AS, et al)(17), Iran(Momen Ali Akbar et al)(25), Kenya(Richard Idro et al)(27),Canada(Dawn S.Hartfield et al)(26) and India(Rajwanti K Vaswani et al)(23) it has been found that there is an association between iron deficiency and occurrence of febrile seizures. Whereas the study done at the University of North Dakota(Kobrinsky NI,et al)(20) Fargo and Iran(Amirsalari et al)(28) shows that iron deficiency was not observed in higher proportion among children with febrile seizures.

Due to conflicting reports between studies on iron deficiency and occurrence of febrile seizures and non-availability of many Indian studies prompted us to do this study.

AIM OF THE STUDY

IV.AIM OF THE STUDY

To study the association between Iron deficiency and the first febrile seizure.

SUBJECTS AND METHODS

V. SUBJECTS AND METHODS

Study Design : Case Control Study

Study Place : Coimbatore Medical College Hospital, Coimbatore

Study Period : March 2010 – December 2010

Study Population : Children getting admitted at pediatric ward CMCH satisfying the criteria for I episode of simple febrile seizure.

Cases **:** Children aged 6 months-5years.

Generalized tonic clonic seizures occurring within 24hours of onset of fever.

Seizures lasting for less than 15 minutes.

Single episode of seizure per febrile illness.

Without any post-ictal neurological deficit.

Controls **:** Children with febrile illness without convulsions

matched by age and sex

Exclusion criteria **:** **Children with Iron supplementation/therapy**

Hematological disorders

Chronic illness

Neurological deficit

Previous history of seizures.

Ratio of cases Vs Controls 1:1

Sample size: From a pilot study, the SD (standard deviation) of Ferritin was found to be 20. In order to detect a difference of 10 with 5% level of significance and 80% power, the sample size needed was 50 in each group.

Sampling Technique: All consecutive children admitted as I episode of febrile seizure were taken for cases and age and sex matched controls were selected from the children admitted with fever in pediatric ward without seizure based on computer generated random sampling technique

Maneuver

After getting informed consent from the parents of cases and controls, they were subjected to detailed history and clinical examination and the findings are entered in the Proforma (Annexure-1)

Blood samples were collected and measures of serum Ferritin (the single most sensitive tool for evaluating the iron status) (21), Hemoglobin (HB), Mean corpuscular volume (MCV) and Mean corpuscular hemoglobin (MCH) are measured and compared.

Serum Ferritin Estimation

Chemiluminescence Immuno Assay for quantitative determination of serum Ferritin. For this 2ml of blood was collected into vacutainers through venipuncture under strict aseptic precautions. Serum is separated from cells by centrifugation. The assay is based on micro plates coated with highly specific anti-ferritin-human antibodies. During the procedure the binding of the analyte, as well as the formation of the sandwich complex and enzymatic color reaction take place during three different reaction phases.

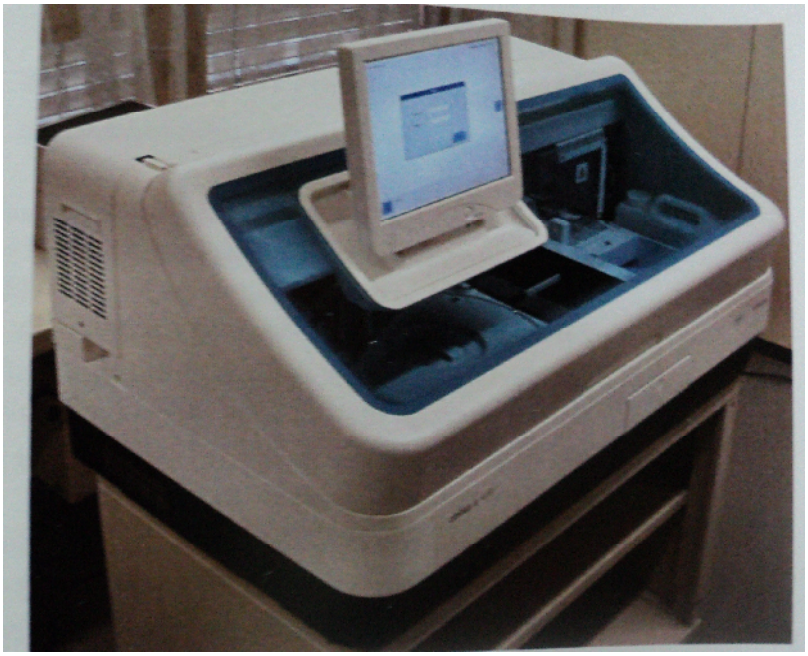
Phase 1:

Calibrators, controls and undiluted patient samples are pipetted together with sample buffer into the wells of the micro plate. Any present

ferritin molecules bind to the inner surface of the wells. After 30 minutes incubation the micro plate is washed with buffer for removing non-reactive serum components.

Phase 2:

An anti-human-ferritin horseradish peroxidase conjugate solution is pipetted into the well of the micro plate to recognize the ferritin bound to the immobilized antibody. After 15 minutes incubation any excessive enzyme conjugate, which is not specifically bound is washed away with wash buffer.



Cobase 411 Analyser (disk system)

Phase 3:

A chromogenic substrate solution containing TMB (3,3,5,5 tetramethyl-benzidine) dispensed into the wells, during 15 minutes of incubation the color of the solution change to blue. Adding hydrochloric acid as stop solution stops color development. The solution color changes into yellow. The amount of color is directly proportional to the concentration of ferritin present in the original sample. The optical density for each calibrator is graphically plotted against the concentration.

Measurement of HB, MCV and MCH are done by using auto-analyzer (Coulter Counter)

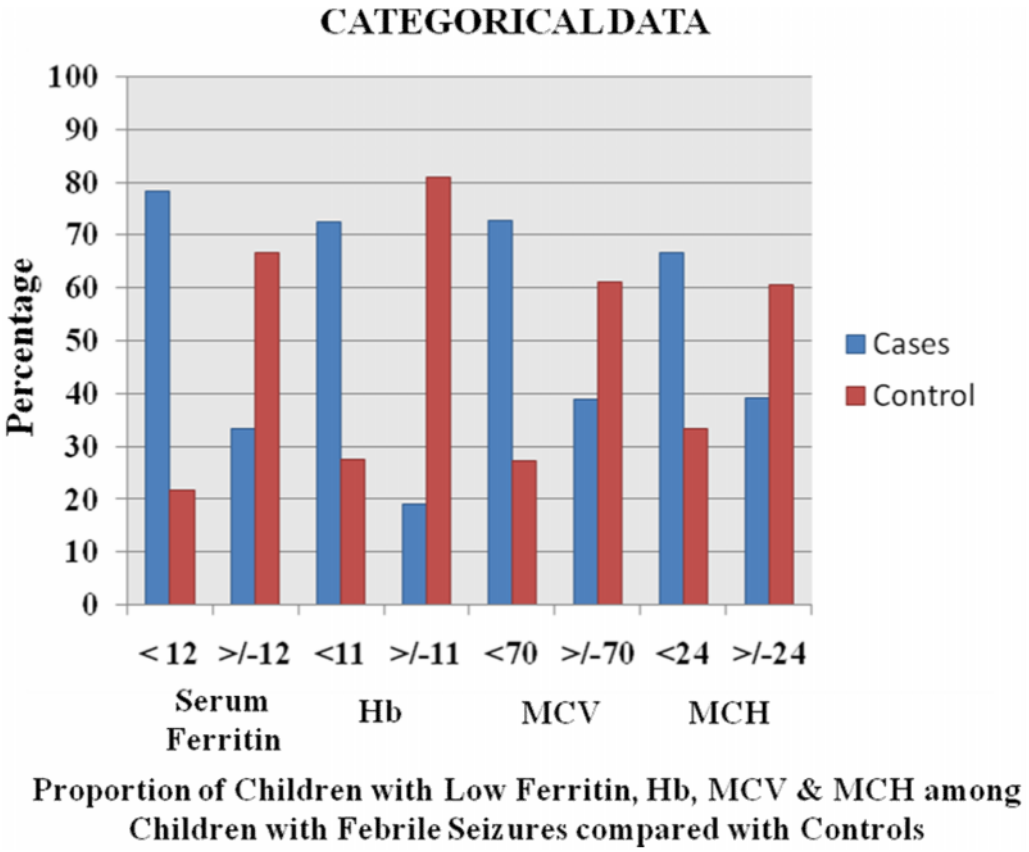
History elicitation, clinical examination and investigations are carried out for cases and controls in similar manner.

STATISTICAL ANALYSIS:

All the data were coded and tabulated for descriptive and inferential statistics. All continuous data were analyzed by the use of t-test or Mann Whitney U test. All proportionate data was analyzed with chi-square or Fischer exact test. SPSS software was used for statistical analysis.

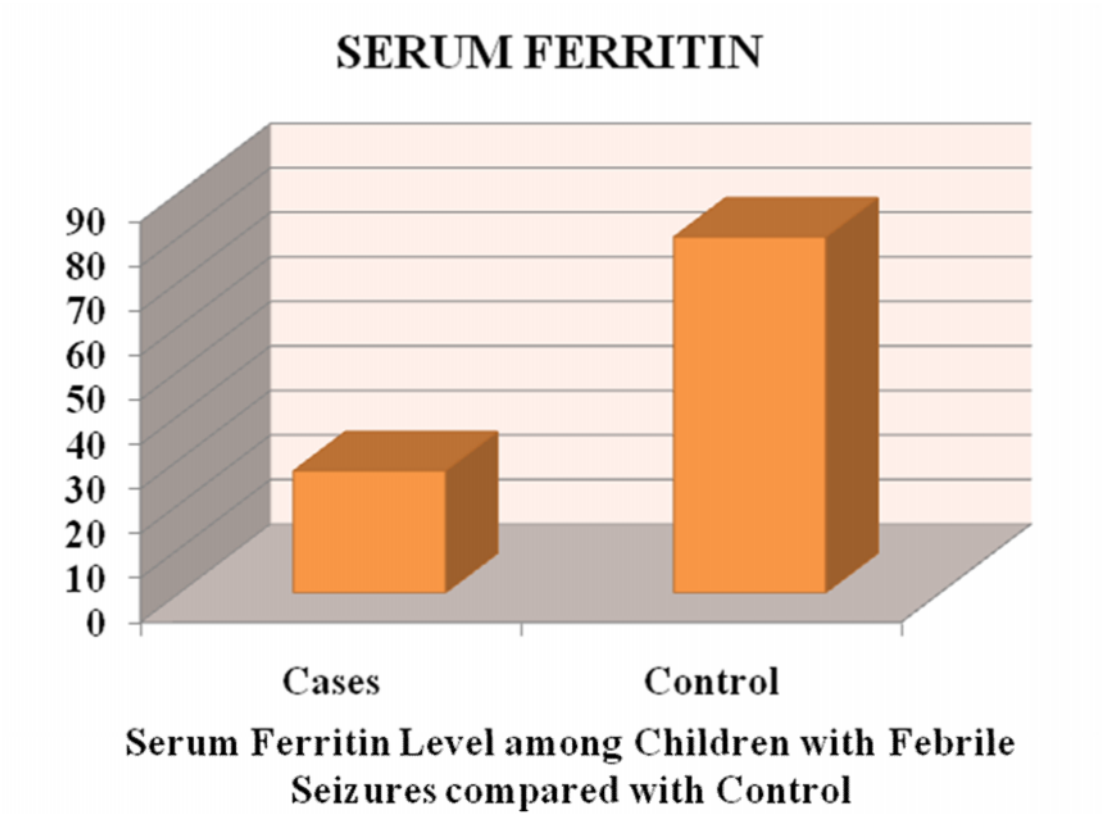
OBSERVATIONS

VI OBSERVATIONS



Proportion of Children with Low Ferritin, Hb, MCV & MCH among Children with Febrile Seizures compared with Controls

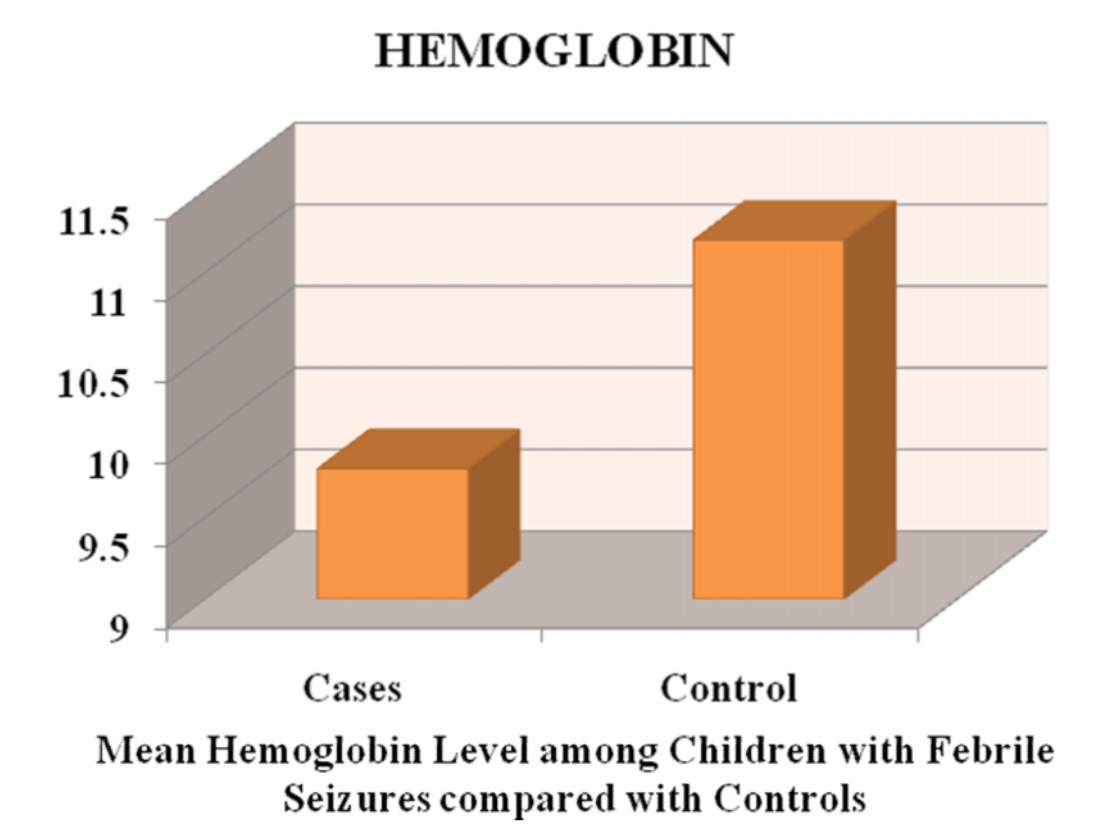
Children with Febrile Seizures having Low Serum Ferritin	:	29
Children with Febrile Seizures having Low Hemoglobin	:	41
Children with Febrile Seizures having Low MCV	:	24
Children with Febrile Seizures having Low MCH	:	23



Serum Ferritin Level among Children with Febrile Seizures compared with Control

The Mean Ferritin Level among Febrile Seizures

Cases	:	27.39 $\pm$ 25.88 ng/ml
Control	:	79.92 $\pm$ 61.91 ng/ml

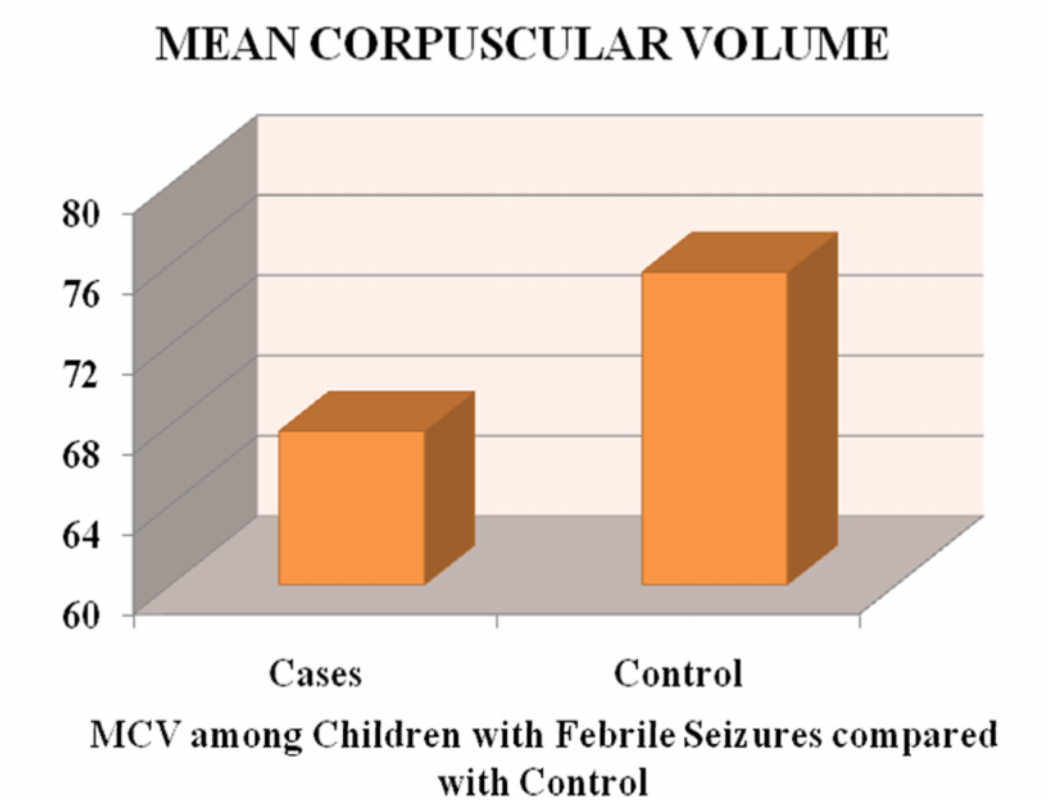


Mean Hemoglobin Level among Children with Febrile Seizures compared with Controls

The Mean Hemoglobin Level among Febrile Seizures

Cases : 9.8 $\pm$ 1.48 gm/dl

Control : 11.2 $\pm$ 1.5 gm/dl

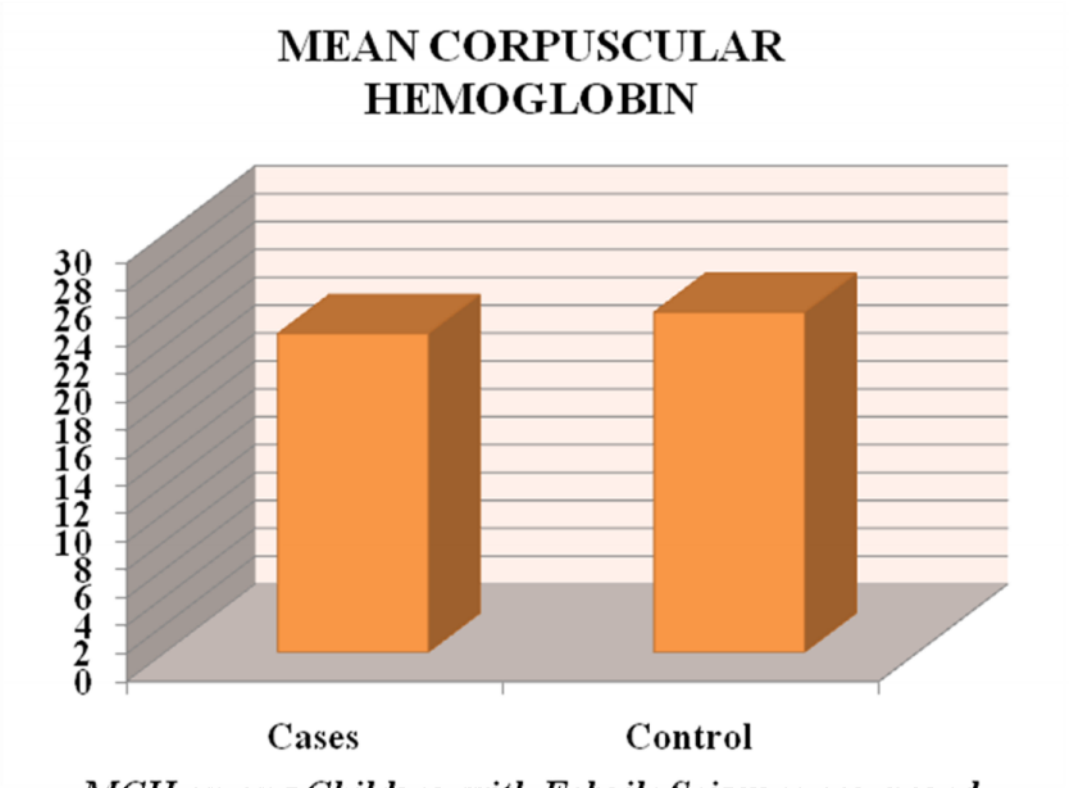


MCV among Children with Febrile Seizures compared with Control

The MCV Level among Febrile Seizures

Cases : 67.67 ± 9.95 fl

Control : 75.6 ± 6.90 fl



MCH among Children with Febrile Seizures compared with Control

The MCH Level among Febrile Seizures

Cases	:	22.86 $\pm$ 3.67 pg
Control	:	24.39 $\pm$ 2.66 pg

VI OBSERVATIONS

Total Cases Studied : 50

Controls Studied : 50

Table – 1&2Incidence of Febrile Seizures with respect to Age &Gender

Table 1 – Age (Months) * Groups

Table 2 – Sex * Groups

A maximum incidence of febrile seizures is found in the age group of 12 months – 24 months (52%) followed by 6 months – 12 months (24%) (Table 1). The incidence of febrile seizures is found to be higher in males (68%) with a male: female ratio of 2:1 (Table 2).

Table – 3 Family History of Febrile Seizures in the two groups

Table 3 – Family History * Groups

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	7.527[b]	1	.006		

Seven children (14%) in the febrile seizures group have positive family history of febrile seizures when compared to none among controls (Table 3). The Chi-Square 7.527 for the association between groups (Cases and Controls). Therefore it can be inferred that there is a strong association between groups and family history.

Table – 4 Mean Value of Serum Ferritin and Blood Indices among those who had Febrile Seizures and Controls

S. No	Variables	Cases		Controls		t Test	P Value
		Mean	SD	Mean	SD		
1.	Sr. Ferritin (ng/ml)	27.39	25.85	79.92	61.91	5.536	0.001
2.	HB (gm%)	9.81	1.41	11.20	1.53	4.722	0.001
3.	MCV (fl)	67.67	9.95	75.66	6.90	4.665	0.001
4.	MCH (pg)	22.86	3.67	24.39	2.66	2.373	0.002

The mean ferritin level among febrile seizures group is found to be 27.39 +/- 25.85 ng/ml whereas in controls it is 79.92 +/- 61.91ng/ml, (P<0.001). The mean Hemoglobin (HB) for cases is 9.81 +/- 1.41 gm/dl, whereas in controls it is 11.2 +/- 1.53 gm/dl, (P<0.001). The Mean Corpuscular Volume (MCV) for cases is 67.67 +/- 9.95 fl and for controls it is 75.66 +/- 6.90 fl, (P<0.001). The Mean Corpuscular Hemoglobin (MCH) for cases is 22.86 +/- 3.67 pg and for controls it is 24.39 +/- 2.66 pg, (P<0.002).

Table – 5 Proportions of Children with Low Serum Ferritin/Blood Indices among Cases and Controls

S. No	Variables		Cases		Controls		P Value
			N	%	N	%	
1.	Sr. Ferritin (ng/ml)	<12	29	58	8	16	0.001
		>12	21	42	42	84	
2.	HB (gm%)	<11	41	82	16	32	0.001
		>11	9	18	34	68	
3.	MCV (fl)	<70	24	48	7	14	0.001
		>70	26	52	43	86	
4.	MCH (pg)	<24	23	46	13	26	0.002
		>24	27	54	37	74	

* Twenty nine children (58%) with febrile seizures have serum Ferritin level <12 ng/ml whereas only 8 children (16%) in control group have Ferritin level<12 ng/ml with a (P<0.001)

* The number of children with haemoglobin <11 gm/dl is 41 (82%) in febrile seizures group whereas among controls it is only 16 (32%) (P<0.001)

* The Mean Corpuscular Volume <70 fl is seen in 24 (48%) cases, whereas in controls it is only 7 (14%) (P<0.001)

* The Mean Corpuscular Hemoglobin <24 is seen in 23 cases (46%) cases, whereas in controls it is only 13 (26%) (P<0.002)

* Thus a significant proportion of children with febrile seizures have low Serum Ferritin, Hemoglobin, Mean Corpuscular Volume and Mean Corpuscular Hemoglobin than did the controls.

Table – 6 Serum Ferritin and Blood Indices among Cases and Controls: Statistical Analysis

Table 6 – Serum Ferritin (ng/ml) * Groups

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	18.919[b]	1	.000		

The Chi-Square 18.919 for the association between groups (Cases and Controls) and levels of Ferritin below (12 ng/ml and above 12 ng/ml) is significant (P<0.001). Therefore it can be inferred that there is a strong association between the Cases and Ferritin Level.

	Groups	N	Mean	Std. Deviation	t test	P Value
S.Ferritin (ng/ml)	Cases	50	27.3902	25.85388	5.536	0.001
	Controls	50	79.9266	61.91778		

Also in the above table, t value 5.536 for the mean difference in the Ferritin level between cases and control group is significant (P<0.001). It reveals that children in cases group have low Ferritin when compared to control group.

Table 7 – Hemoglobin (g/dl) Groups

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	27.750[b]	1	.000		

The Chi-Square 27.750 for the association between groups (Cases and Control) and levels of haemoglobin (less than 11 gm/dl and above 11 g/dl) is significant (P<0.001). Therefore it can be inferred that there is a strong association between the groups and hemoglobin level.

	Groups	N	Mean	Std. Deviation	t test	P Value
Hemoglobin (gm/dl)	Cases	50	9.8120	1.41459	4.722	0.001
	Controls	50	11.2060	1.53522		

In the above table the t value 4.722 for the Mean Difference in the Hemoglobin level between cases and control group is significant (P<0.001). It reveals that the children in cases group have low Hemoglobin when compared to control group.

Table 8 – MCV (fl) Groups

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	10.176[b]	1	.001		

The Chi-Square 10.176 for the association between groups (cases and controls) and levels of Mean Corpuscular Volume (less than 70 fl and above 70 fl) is significant (P<0.001). Therefore it can be inferred that there is a strong association between the groups and Mean Corpuscular Volume.

	Groups	N	Mean	Std. Deviation	t test	P Value
MCV (fl)	Cases	50	67.6720	9.95801	4.665	0.001
	Controls	50	75.6680	6.90686		

In the above table, t value 4.665 for the mean difference in the Mean Corpuscular Volume level between cases and controls group is significant (P<0.001). It reveals that children in cases group have low Mean Corpuscular Volume when compared to control group.

Table 9 – MCH (pg) Groups

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	7.104[b]	1	.008		

The Chi-Square 7.104 for the association between groups (cases and controls) and levels of Mean Corpuscular Hemoglobin (less than 24 pg and above 24 pg) is significant (P<0.002). Therefore it can be inferred that there is a strong association between the groups and Mean Corpuscular Hemoglobin.

	Groups	N	Mean	Std. Deviation	t test	P Value
MCH (pg)	Cases	50	22.8680	3.67115	2.373	0.002
	Controls	50	24.3900	2.66192		

In the above table, t value 2.373 for the mean difference in the Mean Corpuscular Hemoglobin level between cases and controls group is significant (P<0.002). It reveals that children in cases group have low Mean Corpuscular Hemoglobin when compared to control group.

DISCUSSION

VII. DISCUSSION

In our study to detect low iron status as a possible risk factor for first febrile seizures 50 cases and 50 age and sex matched controls are studied and analyzed .

- In the present study we found that the peak incidence of febrile seizure occur during one to two years of age and the mean age is 23.26 months. This is comparable to previous studies. The peak age of onset being 14-18 months of age as per Nelson textbook of Pediatrics (22). Berg et al. in his study found that the peak incidence is between 18 and 24 months (12). Similarly Naveedur Rehman et al. reported the peak incidence at 22 Months (18).
- The present study depicts that the incidence of febrile seizures is slightly higher in boys than in girls and the male: female ratio 2:1. This is similar to the study by Berg et al (12), while Naveedur Rehman et al. reported no gender difference in their study (18).
- In our study family history of febrile seizures is seen only in 14% of cases. But Forfar textbook of pediatrics mentions that 50% will have a family history of convulsions and 80% of monozygotic twins are concordant for febrile convulsions (23).

- The mean serum ferritin level in our study is 27.39ng/ml . It is similar to Daoud AS et al. study from Jordan that the mean ferritin level was 29.5ng/ml (17) whereas Rajwanti K Vaswani et al. in his study group from India found that the mean ferritin level was 31.9 ng/ml(24) Similarly Momen Ali Akbar et al. reported a mean ferritin level of 30.3 ng/ml (25).

- Daoud AS et al. in his study found that a significant proportion of children with febrile seizures had only low serum ferritin level (17). The proportion of children with febrile seizures having low hemoglobin, Mean Corpuscular Volume and Mean Corpuscular Hemoglobin were not statistically significant. Similarly Momen Ali Akbar et al . also in his study found lower ferritin in a significant proportion of children with febrile seizures without any significant difference in complete blood count indices (25). Whereas our study demonstrates a statistically significant difference in the proportion of children with febrile seizures have not only low serum ferritin but also low hemoglobin, low Mean Corpuscular Volume and low Mean Corpuscular Hemoglobin. This is similar to the findings reported by Naveedur Rehman et al. in his study at Karachi (18).

This is probably due to the fact that iron deficiency occurs in three stages.

(a) First stage characterized by decreased storage of iron without any other detectable abnormalities.

(b) An intermediate stage of `latent iron deficiency` i.e. iron stores are exhausted, but anemia has not occurred yet.

(c) The third stage is that of overt iron deficiency when there is a decrease in the concentration of circulating hemoglobin due to impaired hemoglobin synthesis.

The children in Western countries if they are iron deficient are mostly in the early stage. So the study done by Daoud AS et al. in Jordan has a significant proportion of children with low ferritin level, without significant difference in Hb, MCV and MCH. Whereas Indian children/children of our neighboring country Pakistan are in the stages of latent or overt iron deficiency. So our study and the study done in Karachi by Naveedur Rehman et al. had a significantly greater proportion of children with not only low serum ferritin but also low Hb, MCV ,MCH and MCV.

As similar to previous studies by Daoud AS et al., Naveedur Rehman et al., Alfredo Pisacan et al., Rajwanti K Vasani et al.,Momen Ali Akbar et al .,Dawn S. Hartfield et al. (17, 18, 19,24,25,26). our study also demonstrates an association between iron deficiency and febrile seizures. Thus iron deficiency is one of the possible risk factor for febrile seizures. Developmental problems, risk of pediatric stroke, the

occurrence of febrile seizures and breath holding spells are perhaps the tip of the iceberg, of the neurological consequences of iron deficiency. With appropriate recognition, treatment or better yet, prevention the neurological sequalae of iron deficiency are entirely preventable and perhaps reversible.

SUMMARY AND CONCLUSIONS

VIII. SUMMARY

- The peak incidence of febrile seizures is between one and two years of age. The mean age being 23.26 months.
- A male preponderance is observed in all age groups with male: female ratio of 2:1
- Family history of febrile seizures is observed in 14% of cases.
- The mean Serum Ferritin, Hemoglobin and Mean Corpuscular Volume are significantly lower in children with febrile seizures as compared to controls.
- Significantly, a greater proportion of children with febrile seizures have low Serum Ferritin (<12ng/ml); low Hemoglobin (<11gm/dl) and low Mean Corpuscular Volume (<70fl) as compared to controls.

CONCLUSION

Plasma ferritin level and blood indices are significantly lower in children with febrile seizures as compared to children without febrile seizures suggesting that iron deficient children are more prone to febrile seizures. A follow-up study of patients found to be iron deficient at the time of a first febrile seizure to determine the incidence of subsequent febrile seizures after treatment for iron deficiency would be of great interest.

ANNEXURE

ANNEXURE 1

PROFORMA

NAME: **IP NO.**

AGE

SEX

ADDRESS

SOCIO-ECONOMIC STATUS

HISTORY

DATE AND TIME OF ONSET OF FEVER

WHETHER SEIZURES OCCURRED WITHIN 24 HOURS

OF ONSET OF FEVER

TYPE OF SEIZURES

DURATION OF SEIZURES

NO. OF EPISODE

ANY POST-ICTAL NEUROLOGICAL DEFICIT

DEVELOPMENTAL HISTORY

FAMILY HISTORY OF SEIZURES

CLINICAL EXAMINATION

HEART RATE RESPIRATORY RATE

BLOOD PRESSURE

TEMPERATURE

HEIGHT WEIGHT

HEAD CIRCUMFERENCE CHEST CIRCUMFERENCE

MID-ARM CIRCUMFERENCE

CENTRAL NERVOUS SYSTEM

CARDIO VASCULAR SYSTEM

RESPIRATORY SYSTEM

ABDOMEN

INVESTIGATIONS

SERUM FERRITIN

HEMOGLOBIN

MEAN CORPUSCULAR VOLUME

MEAN CORPUSCULAR HEMOGLOBIN

ANNEXURE 2

BIBLIOGRAPHY

1. Livingston S. Comprehensive management of epilepsy in infancy, child hood and adolescence. Springfield, IL: Charles C Thomas, 1972.

2. Consensus Development Conference on Febrile Seizures. Proceedings. Epilepsia 1981:2:377—381.

3. Frantzen E, Lennox-Buchthal M, Nygaard A, et al. A genetic study of febrile convulsions. Neurology 1970; 20:909—917.

4. Rantala H, Uhari M. Risk factors for recurrences of febrile convulsions. Acta Neurol Scand 1994:90:207- 210.

5. Sahib El-Radhi AS, Withana K, Banajeh S. Recurrence rate of febrile convulsion related to the degree of pyrexia during the first attack. Clin Pediatr (Phila,) 1986; 25:31 1—3 13.

6. Doose H, Ritter K, Volzke E. EEG longitudinal studies in febrile convulsions. Gen. Aspects Neuropediatr 1983; 14:81-87.

7. Nelson KB, Ellenberg JH. Predictors of epilepsy in children who have experienced febrile seizures. N Engl J Med 1976; 295: 1029—1033.

8. Annegers JF, Hauser WA, Shirts SB, et al. Factors prognostic of unprovoked seizures after febrile convulsions. N Engl J Med 1987; 316:493-498.

9. Camfield P, Camfield C, Gordon K, et al. What types of epilepsy are preceded by febrile seizures? A population-based study of children. Dev Med Child Neurol 1994;36:887—892.

10. Chevrie JJ, Aicardi J. Duration and lateralization of febrile convulsions: etiological factors. Epilepsia 1975;16:781-789.

11. Gastaut H, Poirier F, Payan H, et al. HHE syndrome, hemiconvulsions, hemiplegia, epilepsy. Epilepsia 1959; 1:418—447.

12. Berg AT, Shinnar S, Darefsky AS, et al. Predictors of recurrent febrile seizures. A prospective cohort study, Arch Pediatr Addex Med 1997; 151:371—378.

13. Ellenberg JH, Nelson KB. Febrile seizures and later intellectual performance. Arch Neurol 1978;35: 17—21.

14. Daoud AS, Batchia A, Al-Sheyyab M, et al: Effectiveness of iron therapy on breath holding spells. J. Pediatr 1997;130:547-550.

15. AAP Grand rounds, iron insufficiency a risk factor for febrile seizures 2002, 8(6); 62-63.

16. Febrile convulsions review and update-J pediatr neurol 2002;2(1);22-24

17. Daoud AS, Batchia A, Abu Esctarsh F et al. Iron status: A possible risk factor for first febrile seizures. Epilepsia 2002;43:740-743.

18. Rehman N, Billoo AG. et al. Association between iron deficiency and febrile seizures. J. coll. Physicians surg. Pak.2005; 15(6): 338-340.

19. Pisacane A, Jansone P, Impaliazzo N et al. Iron deficiency anemia and febrile convulsion. Case control study in children under 2 years. Brit Med J. 1996; 313-343.

20. Kobrinsky NL, Jager JY, Cheang Ms, Yats coff RW: Does iron deficiency rise the seizure threshold. Child Neurol. 1995 10 (2) ; 105-109.

21. Park K., Diagnosis of anemia. In: Park Textbook of Preventive and Social Medicine, 17th edition, Park K., Jabalpur, Banarsidas Bhanut; 2002 Nov., pp.424.

22. Micheal V. Johnston, Seizures in Childhood. In: Nelson Textbook of pediatrics, 17th edition, Behrman, Kliegman and Jenson; 2004, pp.1994.

23. JK. Brown and M.O. Regan., Epilepsy. In: Forfar and Arneils Textbook of pediatrics, 5th edition, AGM Campbell and Neil Mc Intosh; 1998, pp. 683.

24. Rajwanti. K Vaswani, Praveen G Dharaskar, Swati Kullkarani and K Ghosh: Iron Deficiency as a Risk Factor for First Febrile Seizure: Indian Pediatrics 2010;47:437-439

25. Momen Ali Akbar MD, Nikfar Roya MD and Karimi babak MD: Evaluation of Iron Status in 9months to 5 years old Children with Febrile Seizures

26. Dawn S Hartfield MD MPH, Jonathan Tan, Jerome Y Yager MD, Rhonda J Rosychuk PhD, Don Spady MD, Christina Haines Msc,

William R Cruig MDCM: Association between Iron Deficiency and Febrile Seizure in Childhood: article from Blood Weekly June 4, 2009, University of Alberta

27. Richard Idro, Samson Gwer, Thomas N. Williams, Tuda Otieno et al: Iron Acute Seizures, Meta analysis from Rural Kenya, Plos one November 2010 – volume 5 – issue 11 – e14001

28. Amirsalari Susan MD, Keihani Doust Zarrin Taj MD, Ahmadi Mostafa et al: Relationship between Iron Deficiency and Febrile Seizures: Iran J Child Neurology volume 14- No1, June 2010

ANNEXURE - III MASTER CHART

CASES								
S.NO	**NAME**	**AGE Years**	**SEX**	**HEMOGLOBIN g/dl**	**MCV fL**	**MCH pg**	**FERRITIN ng/ml**	**FAMILY HISTORY**
1	kishore	2	Mch	12	76	26.1	64.2	
2	priyadharsini	1.5	Fch	8.6	71.4	21.3	11.48	positive
3	sangeevi	1.5	Mch	8.3	59.1	16.7	10.46	
4	Pavithra	2	Fch	8.2	64.5	24	10.78	
5	Sanjay	1.25	Mch	8.4	62.3	24.8	11.56	
6	Sabarish	5	Mch	9.6	71.2	24.7	10.07	positive
7	Barath	3	Mch	13.3	76	26	22	
8	Karuppusamy	3	Mch	10.8	72.9	24.1	38	
9	Fazila	1.25	Fch	9	59.4	22.5	9.4	
10	Ishwaraya	2	Fch	10.1	72	21.4	10.04	
11	Sanash	2	Mch	10	75.8	24.3	40.4	
12	Harikrishnan	11 mon	Mch	11.8	78.8	26.1	68.2	
13	Mohammad Abrash	1	Mch	10.3	56.6	16.4	10.76	
14	Rishkash	I.25	Mch	6.1	55.4	15.2	10.2	
15	Diviyadharsini	2	Fch	10.9	82.3	26.1	30.6	positive
16	Naresh	2	Mch	8.9	59	24.1	9.62	
17	Mahalakshmi	1	Fch	8.5	66.2	19.1	10.78	
18	Sekar	4	Mch	10.1	67.4	24.5	10.23	
19	Ramesh	1.25	Mch	10.3	71.3	20.7	11.4	
20	Sabari	1	Mch	10.8	70.3	28	11.24	
21	Aravind	2	Mch	7.4	72.4	23	10.02	
22	Karthik	2	Mch	7.9	56.4	20.2	11.49	
23	Arun	1	Mch	9.8	72.1	24.3	9.78	
24	Vinoba	2	Fch	9.1	62.7	18.8	10.08	
25	Susimathi	1,5	Fch	8.4	56.9	16.5	7.61	
26	Mohammad Ansari	1.5	Mch	11.9	72.6	23.2	40.95	
27	Nithesh	1.5	Mch	8.9	63.8	24	10.38	
28	Vikash	2	Mch	9.7	63.8	19.2	10.74	
29	Naren Kumar	8 mon	Mch	10.3	74.7	23.7	55.47	
30	Perumal Vignesh	1.25	Mch	12.4	83.4	27.8	69.48	

ANNEXURE - III MASTER CHART

CASES								
S.NO	**NAME**	**AGE Years**	**SEX**	**HEMOGLOBIN g/dl**	**MCV fL**	**MCH pg**	**FERRITIN ng/ml**	**FAMILY HISTORY**
31	Krishnaveni	9 mon	Fch	8.2	55.4	20.7	7.04	
32	Vishnu	1.5	Mch	10.3	67	22.4	8.74	
33	Gomathi	4	Fch	10.1	74.2	24.3	78.68	
34	Asiza	2.5	Fch	9.4	62.8	27	29.08	positive
35	Varsha	10 mon	Fch	10.3	66.4	21.8	30.06	
36	Malarvizhi	1	Fch	10.1	66.5	26.1	10.06	
37	Samaaz	7 mon	Mch	10.1	73.7	24.3	33.08	positive
38	Sasuthan	1.5	Mch	11	72.6	24.1	77.91	
39	Pragathi Priya	4	Fch	11.1	79.9	25.7	68.02	
40	Kamalesh	1	Mch	8.5	20.1	12	6.02	
41	Sadhana	1.5	Fch	9.3	75.2	24.7	15.02	
42	Kannan	11 mon	Mch	7.9	67.2	19.8	10.02	
43	Jaganathan	2	Mch	12.7	71	27.2	118.5	positive
44	Pandi Durai	2.5	Mch	9.8	62.3	22	11.47	
45	Abdulla	2	Mch	9.9	70.2	24.7	11	
46	Sugail	3	Mch	9.1	72	19.1	65.06	
47	Ramesh	3	Mch	10.3	66.6	20.7	28.11	
48	Muhesh	4	Mch	11.2	79.4	29.8	46.95	positive
49	Ammar	2	Mch	9.2	61	21.2	10.98	
50	Mahalakshmi	4	Fch	10.3	73.4	29	56.29	

ANNEXURE - III MASTER CHART

CONTROL								
S.NO	**NAME**	**AGE Years**	**SEX**	**HEMOGLOBIN g/dl**	**MCV fL**	**MCH pg**	**FERRITIN ng/ml**	**FAMILY HISTORY**
1	Dhanaraj	2	Mch	11.2	82.3	26.1	70.24	
2	Meena Raghini	2	Fch	11.1	81.8	24.3	96.28	
3	Saraj	2	Mch	11.7	75.4	24.1	58.25	
4	Lavanya	2	Fch	8	73.6	23.5	30.28	
5	Srivasanth	1	Mch	9.2	70.2	21.1	11.28	
6	Sudalai Muthu	5	Mch	11	74	24.3	98.76	
7	Aravind	2.5	Mch	13.3	79	27	162.2	
8	Abudhakir	3.5	Mch	11.8	99.5	32.2	178.28	
9	Madhu Sri	1.5	Fch	13.3	74.5	25.6	100.34	
10	Nithya Sri	2	Fch	11.2	78.9	24.8	134.28	
11	Priya	2.5	Fch	11.6	76.2	24.4	264.2	
12	Mohammad Sajmal	10 mon	Mch	12.1	86.9	28.1	128.2	
13	Yogeswaran	1	Mch	9.3	64	20.4	10.28	
14	Yogu	1.5	Mch	9.7	63.8	19.2	11.4	
15	Fathima	2	Fch	9.6	64	20.4	11.7	
16	Dharan	2	Mch	11.9	72.6	24.2	56.08	
17	Lavanya	1	Fch	12.3	76.4	24.6	112.08	
18	Prabhu	4.5	Mch	12	75.8	25.2	98.08	
19	Mohammad Imran	2.5	Mch	8.5	66.2	19.1	1o.26	
20	Irfan	1	Mch	12.9	81.3	26.8	84.26	
21	Kavesh	1.5	Mch	13.1	76.4	26.4	269.9	
22	Nithish	2	Mch	12.1	75.6	25.7	68.4	
23	Mohammad Nafiz	10 mon	Mch	11.2	73.2	23.4	37.4	
24	Anisya	2	Fch	12.6	79.3	26.6	178.9	
25	Sugumari	1.5	Fch	14.3	75.4	24.4	94.26	
26	Madhan	2	Mch	13.3	74.5	24.6	149.78	
27	Mohammad Yusuf	1.5	Mch	12.8	79	27	86.08	
28	Karthikeyan	2	Mch	9.5	86.9	25.6	18.08	
29	Subramani	1	Mch	9.9	80.8	26.8	36.28	
30	Mohammad Sukil	1.5	Mch	11.8	81.7	27.7	94.28	

ANNEXURE - III MASTER CHART

CONTROL								
S.NO	**NAME**	**AGE Years**	**SEX**	**HEMOGLOBIN g/dl**	**MCV fL**	**MCH pg**	**FERRITIN ng/ml**	**FAMILY HISTORY**
31	Mangyarharsi	1.25	Fch	9.8	69.1	20.3	10.76	
32	Ajmal	1.75	Mch	12	86.9	27	144.28	
33	Sahana	4	Fch	11.6	80.7	25.9	64.28	
34	Sathya	2	Fch	11.6	75.5	25.5	76.28	
35	Nisanth	9 mon	Mch	12.9	81.3	26.8	72.8	
36	B/O Bhuvaneswari	10 mon	Fch	11.3	72.5	25.1	14.28	
37	Akash	1	Mch	8.2	83.3	24.8	72	
38	Rajan	1.5	Mch	11.7	72.4	25.3	64.28	
39	Shalini	3	Fch	12.7	74.6	24.1	58.08	
40	Shekmohammad	1	Mch	12.9	81.3	26.8	148.23	
41	Rajeswari	1.5	Fch	9.6	64	20.4	31.08	
42	Rohit	11 mon	Mch	10.4	66.1	21.2	34.28	
43	Sagaputheen	2	Mch	10.4	71	21.8	28.04	
44	Ellakiya	2	Fch	11.2	74.2	24.4	48.4	
45	Senthil	2.5	Mch	8.7	66.4	19.3	10.07	
46	Vishnavi	3	Fch	11.4	72.4	24.2	26.7	
47	Anvar	3.5	Mch	11.1	75.1	24.3	89.2	
48	Ashik	3.5	Mch	11.4	75.2	24.7	142	
49	Rasith	1	Mch	11.3	73	24.1	89.2	
50	Abinaya	4	Fch	7.8	69.2	19.9	12	