“PROSPECTIVE AND OBSERVATIONAL STUDY ON ROLE OF MRI IN ACUTE FEBRILE ENCEPHALOPATHY IN CHILDREN”

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115

LIST OF ABBREVIATIONS

HE	Hepatic encephalopathy
AFE	Acute febrile encephalopathy
PRES	Posterior reversible encephalopathy syndrome
CTE	Chronic traumatic encephalopathy
MELAS	Mitochondrial encephalopathy, lactic acidosis & stroke like episodes
DNA	Deoxyribonucleic acid
CBC	Complete blood count
CT	Computed tomography
MRI	Magnetic resonance imaging
JE	Japanese encephalitis
HHV	Human herpes virus
PML	Progressive multifocal leukoencephalopathies
SSPE	Subacute sclerosing panencephalitis
HUS	Haemolytic uremic syndrome
ADEM	Acute demyelinating encephalomyelitis
ANE	Acute necrotizing encephalopathy
AESD	Acute encephalopathy with biphasic seizures and late reduced diffusion
AIEF	Acute encephalopathy predominantly affects frontal lobes
LP	Lumbar puncture
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
CS	Culture and sensitivity

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF IMAGES

ABSTRACT

Background: Acute febrile encephalopathy (AFE) in children is a medical emergency and could be a manifestation of many systemic and central nervous system pathologies as well. The clinical features of AFE are nonspecific and etiological spectrum variable depending on the studied population. The changes in MRI would help us to analyse the associated functional abnormalities.

Objectives: To analyze the correlation between the severity of CNS signs, symptoms and the extent of lesions on MRI acute febrile encephalopathy in children and to analyze the variation in lesions found on MRI among different etiology of acute febrile encephalopathy in children.

Methodology: Prospective observational study for one year, including 31 cases of acute febrile convulsion with disorientation but excluding the cases of head injury and not willing to be part of the study. All the subjects underwent MRI imaging. Due to time constraint only the cases with MRI changes were analysed.

Results: Incidence of patients aged 11 years was higher, accounting for about 35.5% of the cases. 17(54.8%), while the rest of the 14 (45.2%) were males. Most common symptoms was irritability in 18 (58.1%) patients followed by Loose stools in 11 (35.5%). Viral encephalitis was the commonest diagnosis. modified Rankin score of 2 in 14(45.2%) of the patients or a score of 3 in 12 (38.7%) of the patients. The outcome was better irrespective of the score. Bilateral periventricular and peritrigonal region was the commonest MRI changes we observed with the incidence of about 16.1% (5/1). There was no association between the MRI changes and modified Rankin score and specific symptoms.

Conclusion: As the frequency of various MRI changes being observed among 31 cases in one year, this is comparatively higher. Hence, there is need for more such clinical study data to observe the epidemiology of acute febrile encephalopathy and related brain changes.

INTRODUCTION

Encephalopathy is a disease state in which higher brain activities are affected due to metabolic disturbances. It is characterized by global cerebral dysfunction without any structural abnormalities in the brain[1]. Metabolic homeostasis greatly influences the neuron activities and working of the brain. Thus, any abnormality or variation of the metabolic systems will lead to brain disorders and can result in clinical and electroencephalographic variations[1].

In some cases, these changes are reversible and in other cases, they are not. Metabolic encephalopathy is characterized by the general deterioration in the brain functioning caused due to failure of major organs of the body like liver, kidney or due to electrolytic imbalances. Encephalopathy caused due to acute or chronic renal failure is termed renal or uremic encephalopathy[2,3]. It is presented with alterations in mental status varying from mild sensorial clouding to delirium or coma state or motor disturbances. This type of encephalopathy is developed in patients with acute or chronic renal failures, but the encephalopathy symptoms are progressed rapidly in patients with acute renal failure. The symptoms of uremic encephalopathy are non-specific, variable and due to multiple metabolic derangements. In uremic encephalopathy, the balance between excitatory and inhibitory neurotransmitters is affected due to the accumulation of uremic toxins accumulated due to renal failure[4,5]. This reduces the metabolic activity of brain and decreases oxygen consumption.

Encephalopathy caused due to liver dysfunction or due to liver diseases like hepatitis or cirrhosis is termed hepatic encephalopathy[6-8]. It is a neuropsychiatric syndrome and symptoms varying from subtle memory loss or attention deficit to deep coma state. Hepatic encephalopathy (HE) is usually metabolically induced, when liver fails to perform its detoxifying action. It can also occur due to portosystemic shunts which circulate the portal blood before removal of toxins by the liver. Ammonia neurotoxicity is the primary cause for hepatic encephalopathy where ammonia is not quickly converted to urea due to liver malfunctioning, thus causing ammonia to accumulate in the blood. Ammonia is produced due to the deamination of amino acids during protein metabolism and also by the intestinal bacteria. Thus, HE is a secondary disease affecting brain due to liver disease or portosystemic shunting.

Encephalopathy due to low sugar level in the blood is termed hypoglycemic encephalopathy[1]. It occurs when the rate of glucose entering for systematic circulation is reduced, as compared to its uptake by the tissues. Brain is primarily affected when glucose level is reduced as it is the primary metabolic fuel. This will result in slow reaction of the patient, loss of consciousness, blurred speech and degradation of other cognitive functions[9].

Hypocalcemia is a type of encephalopathy caused due to low level of calcium in the blood. The major causes are hyperparathyroidism and vitamin D deficiency. It is highly epileptogenic and causes slowed EEG and generalized bursts of spikes. They get improved when normal calcium levels are restored. Hypercalcemia is caused due to increased level of calcium in the blood, which can weaken the bones, create kidney stones and can eventually affect heart and brain. It occurs mainly due to hyperparathyroidism; when over active parathyroid glands produce too much hormones resulting in increased level of calcium in the blood.

Encephalopathy caused due to low levels of sodium level in the blood is called hyponatremia. Higher levels of sodium in the blood lead to hypernatremia. Thus, cerebral activity is affected in metabolic encephalopathy in the absence of gross structural abnormalities of the brain. Metabolic encephalopathy can therefore be considered as a secondary neurological disease as brain is not primarily affected in this disease. Acute febrile encephalopathy (AFE) in children is a medical emergency and could be a manifestation of many systemic and central nervous system pathologies. The clinical features of AFE are nonspecific and etiological spectrum variable depending on the studied population[10].

AIMS & OBJECTIVES

Primary objective:

Analyzing the role of MRI in identifying the acute febrile encephalopathy in children.

Secondary objectives:

- To analyze the correlation between the severity of CNS signs, symptoms and the extent of lesions on MRI acute febrile encephalopathy in children.
- To analyze the variation in lesions found on MRI among different etiology of acute febrile encephalopathy in children**.**

REVIEW OF LITERATURE

ENCEPHALOPATHY

Encephalopathy is a term that refers to brain disease, damage, or malfunction. In modern usage, encephalopathy does not refer to a single disease, but rather to a syndrome of global brain dysfunction; this syndrome can have many different organic and inorganic causes. Encephalopathy can present a very broad spectrum of symptoms that range from mild, such as some memory loss or subtle personality changes, to severe, such as dementia, seizures, coma, or death[11].

In general, encephalopathy is manifested by an altered mental state that is sometimes accompanied by physical manifestations (like; poor coordination of limb movements). The term encephalopathy, in most cases, is preceded by various terms that describe the reason, cause, or special conditions of the patient that leads to brain malfunction. For example, anoxic encephalopathy means brain damage due to lack of oxygen, hepatic encephalopathy means brain malfunction due to liver disease and A child presenting with fever, altered cognition or personality, and altered sensorium and/or seizure is labelled as acute febrile encephalopathy (AFE). Additionally, some other terms either describe body conditions or syndromes that lead to a specific set of brain malfunctions. Examples of these are metabolic encephalopathy and Wernicke's encephalopathy[12,13]. There are over 150 different terms that modify or precede "encephalopathy" in the medical literature.

CAUSES OF ENCEPHALOPATHY

The causes of encephalopathy are both numerous and varied. Some causes of encephalopathy include:

- Infectious (bacteria, viruses, parasites, or prions),
- Anoxic (lack of oxygen to the brain, including traumatic causes),
- Alcoholic (alcohol toxicity),
- Hepatic (liver failure or liver cancer),
- Uremic (renal or kidney failure),
- Metabolic diseases (hyper or hypocalcaemia, hypo or hypernatremia, or hypo or hyperglycemic),
- Brain tumors (pathological, accidental),
- Many types of toxic chemicals (mercury, lead, or ammonia),
- Alterations in pressure within the brain (often from bleeding, tumors, or abscesses),
- Poor nutrition (inadequate vitamin B1 intake or alcohol withdrawal).

These examples do not cover all of the potential causes of encephalopathy but are listed to demonstrate the wide range of causes[14]. Although numerous causes of encephalopathy are known, the majority of cases arise from several major categories (some examples in parentheses):

- Infection (HIV, Neisseria meningitides, herpes, hepatitis B and hepatitis C),
- Liver damage (alcohol and toxins),
- Brain anoxia or brain cell destruction (trauma and toxic chemicals), and
- Kidney failure (uremic).

Some drugs may cause encephalopathy; for example, posterior reversible encephalopathy syndrome (PRES) may occur due to the use of drugs like tacrolimus and cyclosporine. This syndrome manifests with symptoms of headache, confusion, and seizures.

SYMPTOMS OF ENCEPHALOPATHY

Despite the numerous and varied causes of encephalopathy, at least one symptom present in all cases is an altered mental state. The altered mental state may be subtle and develop slowly over years (for example, in hepatitis the decreased ability to draw simple designs, termed apraxia) or be profoundly obvious and develop rapidly (for example, brain anoxia leading to coma or death in a few minutes). Often, symptoms of altered mental status can present as inattentiveness, poor judgment, or poor coordination of movements. Other serious symptoms that may occur include:

- lethargy,
- dementia,
- seizures,
- tremors,
- muscle twitching and myalgia,
- Cheyne-Stokes respirations, and
- Coma.

Often the severity and type of symptoms are related to the severity and cause of the brain disease or damage. For example, alcohol-induced liver damage (alcoholic cirrhosis) can result in involuntary hand tremors (asterixis), while severe anoxia (lack of oxygen) may result in coma with no movement. Other symptoms may not be as severe and be more localized such as cranial nerve palsies (damage to one of the 12 cranial nerves that exit the brain). Some symptoms may be very subtle and result from repeated injury to the brain tissue. For example, chronic traumatic encephalopathy (CTE), due to injury like concussions repeatedly sustained by football players and others who play contact sports, may cause slow changes over time that are not easily diagnosed. Such injury may lead to chronic depression or other personality changes that can result in life changing consequences[15].

Even infants and children can suffer encephalopathy; similar symptoms can occur in the prenatal period if, for any reason like high fever and in neonate if they had any compromise to brain blood flow during its development. Rasmussen's encephalitis is a rare disease that is seen in children that progresses to intractable seizures if untreated; it may be due to autoantibody development[16]. Another rare form of encephalopathy that usually develops in younger people (about ages 4 to 20 years) is the mitochondrial encephalopathy, lactic acidosis, stroke-like episodes (MELAS syndrome) due to faulty deoxyribonucleic acid (DNA) in the patient's mitochondria.

DIAGNOSIS OF ENCEPHALOPATHY

The diagnosis of encephalopathy is usually done by clinical tests done during the physical examination (mental status tests, memory tests, and coordination tests) that document an altered mental state[17]. With most cases, findings on clinical tests either diagnose or presumptively diagnose encephalopathy. Usually, the diagnosis occurs when the altered mental state accompanies another primary diagnosis such as chronic liver disease, kidney failure, anoxia, or many other diagnoses.

Consequently, physicians may utilize several different tests at the same time to diagnose both the primary condition (the cause of encephalopathy) and the encephalopathy itself. This approach to diagnosis is done by most physicians, because many doctors view encephalopathy as a complication that occurs because of a primary underlying health problem. The most frequently utilized tests are listed below with some of the major primary causes of the same.

- Complete blood count or CBC (infections or loss of blood)
- Blood pressure (high or low blood pressure) Metabolic tests (blood levels of electrolytes, glucose, lactate, ammonia oxygen, and liver enzymes)
- Drugs or toxin levels (alcohol, cocaine, amphetamines, and many others)
- Blood and body fluid cultures and analyses (infections of many types)
- Creatinine (kidney function)
- Computed tomography (CT) and magnetic resonance imaging (MRI) scans (brain swelling, anatomical abnormalities, or infections)
- Doppler ultrasound (abnormal blood flow to tissues or abscesses)
- Encephalogram (EEG) (brain damage or abnormal brain wave patterns)
- Autoantibody analysis (dementia caused by antibodies that destroy neurons)
- Review of the person's medications as some medications (for example, cyclosporine) may be responsible for symptoms

This list is not exhaustive, and not all of the above tests need to be done to reach a diagnosis.

ACUTE FEBRILE ENCEPHALOPATHY

Acute febrile encephalopathy (AFE) is defined in children, if a child is presenting with fever, altered cognition or personality, and altered sensorium and/or seizure. It is a medical emergency as well as a diagnostic and therapeutic challenge for the pediatrician[1.] A subset of such patients with evidence of inflammation of brain parenchyma, either infectious or noninfectious, is called as encephalitis[19].

Limited literature in children suggests CNS infections to be the most common cause of AFE in India[20-23]and other developing countries[24-26] though there has been a great variation in the frequency of different contributing etiologies across the globe and even different regions within a country. The nonspecific nature of clinical features further makes the clinical prediction of possible etiology very difficult in cases of AFE; which in turn, may lead to a delay in institution of appropriate therapy.

The paucity of data on risk factors associated with AFE in children is also well appreciated[20].AFE was defined as acute onset (≤14 days) fever (axillary temperature >35.5°C or 95.5°F) with altered state of consciousness lasting for ≥12 h and/or seizure. AFE, though a rare diagnosis in children, is associated with significant morbidity and high mortality, particularly in a developing country like India.

With nonavailability of many pathogen-specific microbiological investigations, etiological agent may remain elusive in a considerable proportion of cases. Nevertheless, many cases being viral in origin, where no specific treatment is available or highly effective, early institution of aggressive supportive care may be able to decrease mortality and long-term morbidity[20].

Incidence of Acute Febrile Encephalopathy

The incidence of acute febrile encephalopathy is reported all over the world with viruses being the most common etiology. The incidence is approximately 0.9 per 100,000 adults in Nigeria, to 185 per 100,000 adults in Nepal during an outbreak of Japanese encephalitis. In India, it has been estimated that a population of 135 million people residing in 171 endemic districts of 17 states are at risk of AFE.

Most of the disease burden is from Uttar Pradesh. JE was the most common cause for AFE in India and it remains to be the most common cause. The profile of acute febrile encephalopathy varies across different geographic regions with newer agents being increasingly recognized all over the world. The geographical variation may be attributable to the transmission by arthropods. Due to the diversity of causes and large number of similar conditions, it's a challenge to the physicians as this syndrome has better outcome when early diagnosis and prompt treatment is done[25].

Epidemiology

Acute febrile encephalopathy has wide range of causes. Viral, bacterial, parasitic, fungal or rickettsial and the spectrum varies with geography and seasonally. Epidemics are caused by single agent, sporadic cases are likely to be caused by multiple etiologies. Epidemics in India are mostly caused by Japanese encephalitis virus and have predominantly affected children.

Bacterial meningitis in developed nation is 2-5/100000 and 10 times higher in developing nations. Herpes simplex encephalitis is the common sporadic encephalitis, while Japanese encephalitis is the endemic encephalitis in the world and is prevalent in South East Asia. But the cause of acute febrile encephalopathy in India has changed in the previous decade and both epidemic investigations and the surveillance of endemic cases have reported non-Japanese encephalitis etiology[27].

Classification of Acute Encephalopathy[27]

Microbiological classification	• Influenza-associated encephalopathy • Human herpesvirus (HHV)-6/7 encephalopathy • Rotavirus encephalopathy • Respiratory syncytial virus encephalopathy • Herpes simplex virus encephalopathy • Varicella-zoster virus encephalopathy • Progressive multifocal leukoencephalopathies (PML) associated with the HIV virus such as subacute sclerosing panencephalitis (SSPE) caused by the measles virus and subacute encephalitis caused by the rubella virus. Bacterial infection-associated encephalopathy (Acute encephalopathy associated with hemolytic uremic syndrome (HUS) caused by *E. coli* O157:H7 and rotavirus infection and salmonella infection) [22] • Encephalopathy caused Bacillus cereulide-producing Bacillus cereus. • Mycoplasma infection-associated encephalopathy • Acute disseminated encephalomyelitis (ADEM) • Others
Metabolic errors	• Classic Reye syndrome • Encephalopathy secondary to inherited metabolic disorders (acute metabolic encephalopathy with carbamoyl phosphate synthetase 1 deficiency) [23]
Cytokine storm	• Encephalopathy with diffuse brain swelling Rey-like syndrome, sepsis-like encephalopathy) • Hemorrhagic shock and encephalopathy syndrome (HSES) • Acute necrotizing encephalopathy (ANE) • Non-herpetic limbic encephalitis (NHLE)
Excitotoxicity	• Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) • Acute infantile encephalopathy predominantly affects the frontal lobes (AIEF) • Hemiconvulsion–hemiplegiaepilepsy syndrome (HHE) • Anti-N-methyl-D-aspartate receptor encephalitis
Unknown or others	• Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) • Posterior reversible leukoencephalopathy syndrome (PRES or RPLS) [24] • Febrile infection-related epilepsy syndrome (FIRES) synonym: acute encephalitis with refractory, repetitive partial seizures (AERRPS) • Acute cerebellitis/cerebellopathy [25] • Epileptic encephalopathies with child onset • Acute encephalopathy with a background of genetic abnormalities in the early neonatal period (NEXMIF gene abnormality, Biallelic TBCD Mutations, mutations in ARX genes) [20,26] • Dravet syndrome • Acute encephalopathy associated with congenital adrenal hyperplasia (CAH) • Unclassified encephalopathy

Acute Febrile Encephalopathy- Clinical Presentation

A pathologic feature of acute encephalopathy is non-inflammatory brain edema. This pathologic feature increases intracranial pressure, which leads to decreased cerebral perfusion pressure and eventually herniation syndromes and/or brainstem dysfunction associated with central nervous system-caused respiratory and circulatory failure[28,29]

Seizures are common in many people, and they are often febrile and last for a long time (febrile status epilepticus). Depending on the child's age, there may be a change in personality or behavior as well as a decrease in cognitive functioning, developmental regression/stasis, a reduction in conscious level, and specific localizing features such as seizures, ataxia, tremor, or other focal motor symptoms. Fever, vomiting, lethargy, loss of appetite, and headache are all examples of systemic symptoms.

Regardless of the cause of encephalopathy, all cases of acute encephalopathy have at least one symptom, namely an altered mental state. The altered mental state can be subtle and develop over time, such as apraxia, or the inability to sketch simple drawings, or it can be obvious and develop quickly, leading to coma or death within minutes[30]. The clinical course of metabolic errors and inherited metabolic disorders may include gradually progressive or static features, followed by the emergence of an acute encephalopathic crisis, including lethargy, behavioral changes, or gait disturbances caused by infections or a fasting state. Patients presenting with a cytokine storm may have systematic inflammatory response syndrome, which includes –

(1) increased or depressed leukocytes or 10% immature neutrophils,

(2) tachycardia or bradycardia,

(3) tachypnea or the need for mechanical ventilation, and

(4) Elevated or depressed leukocytes or 10% immature neutrophils.

Acute excitotoxic encephalopathy, a mild encephalopathy caused by excitotoxicity is defined as a loss of consciousness that lasts more than 24 h and is usually accompanied by seizures but does not have a biphasic clinical course[31].

Selected causes of febrile encephalopathy in children

Febrile encephalopathy with meningeal irritation
- Meningitis
- Meningo –Encephalitis
- Acute disseminated encephalomyelitis

Febrile encephalopathy without meningeal irritation*
- Infectious encephalopathies: Shigella encephalopathy, Enteric encephalopathy, Cerebral malaria, dengue, Rickettsial: Lyme disease, Rocky mountain spotted fever
- Systemic Infections: severe gram-negative sepsis, toxic shock syndrome
- Infections with complications such as Stroke, Venous thrombosis, metabolic derangements (fluid &electrolyte disturbances (dehydration, hyponatremia, hypernatremia, hypoglycaemia)
- Metabolic disorders: (decompensated or precipitated by the intercurrent infection):, Diabetic keto-acidosis, Reye syndrome, inborn errors of metabolism
- Organ failures with intercurrent infections: Uremia, Hepatic failure
- Post infectious disorders: Acute disseminated encephalomyelitis, Hemorrhagic shock and encephalopathy syndrome
- Post immunization encephalopathy: Whole cell pertussis vaccine, Semple Rabies vaccine
- Drugs and toxins- Anticholinergics
- Post prolonged convulsive status epilepticus
- Heat stroke

*Remember that infants and severely ill children may not have meningeal signs despite a meningeal infection or inflammation

.Diagnosis

A coma with obvious consciousness impairment or a convulsive condition is a clinical indicator of acute encephalopathy; however, identifying acute encephalopathy in these circumstances is fairly easy. However, there are various early signs and symptoms as well as variations in these symptoms. This large range of clinical symptoms mirrors the wide range of cerebral function abnormalities as provided by the International Encephalitis Consortium, which recommends the diagnosis of encephalitis and encephalopathy of presumed infectious or autoimmune etiology. An altered mental state is a major criterion.

Additional criteria (minor) to substantiate diagnosis include fever ≥38 ◦C (100.4 ◦F) within the 72 h before or after presentation; generalized or partial seizures not fully attributable to a pre-existing seizure disorder; new onset of focal neurological findings; cerebrospinal fluid (CSF) white blood count ≥5 mm3 ; and electroencephalographic abnormality that is consistent with encephalopathy and not caused by another factor or and not caused by another condition[32].

A clinical examination and a management plan for a child with encephalopathy should be developed concurrently. As soon as possible, a full history should be obtained. A thorough neurologic examination should be performed to localize brain damage and evaluate early prognostic indicators as well as to detect systemic symptoms such as rash, lymphadenopathy, and hepatosplenomegaly[33].

During a physical examination, clinical procedures such as mental status tests, memory tests, and coordination tests that record an altered mental state are commonly used to diagnose encephalopathy. Clinical test results are frequently used to diagnose or presumptively diagnose encephalopathy. When the altered mental state occurs associated with another primary disorder, such as chronic liver disease, kidney failure, anoxia, or a variety of other conditions, the diagnosis is typically made[34].

Glucose, ammonia, lactate, and ketone body levels in the blood as well as plasma acid–base status can all be used to help identify the subtype associated with genetic metabolic illnesses. The eventual diagnosis is based on certain laboratory findings at the start and/or during the static periods[35].

EEG is a widely used technique for detecting and monitoring children with acute encephalopathy. Technological advancement has greatly simplified long-term bedside EEG monitoring. EEG has the advantage of being able to examine real-time brain function by recording electrical activity in the brain. Some children with acute encephalopathy are extremely ill and unstable in general. Even under these conditions, EEG monitoring is possible[35].

Several studies on long-term EEG monitoring among critically ill children with reduced consciousness, including those with acute encephalopathy, have recently been published. There have been numerous studies published on conventional EEG findings in children with acute encephalopathy. According to these results, EEG abnormalities are extremely common among children with acute encephalopathy. As a result, EEG is deemed to be useful in diagnosing acute encephalopathy.

These EEG abnormalities include generalized/unilateral/focal slowness, low voltage, periodic lateralized epileptiform discharges, and paroxysmal discharges[36]. EEG has demonstrated its ability to detect non-convulsive status epilepticus in AESD and FIRES/AERRPS (intermittent, latent seizures) [37].

EEG data may aid in differentiating AESD from long-term febrile seizures. Children with prolonged seizures and fever, reduced or absent spindles/fast waves as well as continuous or frequent slowing during sleep are diagnosed with AESD[38]. When combined with the clinical picture in patients with encephalopathy, EEG and brain imaging may improve diagnosis and have prognostic significance.

The most common EEG finding in patients with encephalopathy is isolated persistent slowing of background activity. These patterns are linked to a variety of structural and non-structural pathologies. The analysis of CSF is critical for determining the cause of encephalitis and distinguishing it from other types of encephalopathy. Lumbar puncture (LP) should be performed as soon as possible in suspected cases of encephalitis unless contraindicated[38].

Clinical evaluation rather than cranial computerized tomography (CT) should be used to determine whether or not an LP is safe to perform[39]. Increased total protein and CSF/serum albumin quotient levels may be linked to severe edema[40]. Increased levels of cytokines and chemokines in CSF and serum may indicate an overly aggressive immune response[41]. CSF examination may reveal pleocytosis in some disorders[42], whereas pleocytosis may be uncommon in others.

Since 2000, imaging technology such as CT, MRI, SPECT, PET, and a variety of other neuroradiological tools have been used to treat heterogeneous acute encephalopathy syndrome. Acute febrile encephalopathy was first defined using neuroradiographic images and clinical data derived from imaging, and it has since advanced significantly. It was possible to see fine cerebral edema images in acute encephalopathy. When acute encephalopathy is suspected, CT is usually the first test performed, because it is available in the majority of Japanese regional centers and has a quick imaging time. Acute encephalopathy is identified by cranial CT abnormalities[35], which include:

(1) low-density zones spanning the entire brain or possibly the entire cerebral cortex,
(2) no clear distinction between the cerebral cortex and the limbic system medulla,
(3) both the surface of the cerebral subarachnoid space and the ventricles becoming narrower,
(4) areas of low density: bilateral thalamus (ANE) and unilateral cerebral hemisphere (in some cases of AESD),
(5) narrowing of the brain's surrounding cisterns: swelling of the brainstem

In some cases, a CT scan can be used to diagnose severe encephalopathy (for example, HUS encephalopathy), which has more edema in the brain than in mild cases[43]. MRI, in contrast, is a sensitive and non-radiological method for detecting encephalopathy, with diffusion-weighted imaging (DWI) being especially helpful in detecting early abnormalities. High-intensity lesions were either visible only on b = 3000 DWI for AESD, MERS, HSE, and unclassifiable encephalopathy or effectively identified on b = 3000 DWI than on b = 1000 DWI. The classifications of acute encephalopathy with febrile convulsive status epilepticus (AEFCSE), acute infantile encephalopathy [AIEF], and Acute encephalopathy with biphasic seizures and late reduced diffusion [AESD] are all part of a single spectrum and may refer to the same condition.

On MRI diffusion-weighted images, a clinical form of AESD that specifically disrupts frontal lobe function in infants has been reported. As a result, the concept of AIEF is intended to be included in AESD: unlike AEFCSE, which has a biphasic course after a relatively short convulsive overlap, AESD has a biphasic course after a relatively short convulsive overlap, i.e., an initial febrile convulsive overlap followed days later by an afebrile partial convulsion with abnormal onset on MRI images.

There is no English literature on AEFCSE. In Japan, there was controversy based on cases of frontal lobe dominance with a course similar to AESD, whereas AEFCSE was a concept focused on the encephalopathy of the convulsive superimposed form of AESD. Since then, it has been determined that these three concepts are nearly identical to the AESD concept.

MRI is better at defining the extent and severity of involvement in neuroinfections and other non-infectious conditions of the brain. Diffusion-weighted imaging (DWI) detects lesions early in patients with viral encephalitis, and in cases with parenchymal complications of meningitis. It is of help in differentiation of pyogenic abscess from other ring-enhancing lesions. It provides evidence of fronto-temporal pathology in herpes simplex encephalitis, thalamic involvement in Japanese-B encephalitis, demyelination in ADEM, or necrotizing lesions in acute necrotizing encephalopathy[44].

MRI is superior to CT in early detection of signs of Herpes encephalitis, which can be demonstrated within the first 48 hours on T2WI or FLAIR images[45]. Magnetic resonance imaging of EV71 encephalitis typically shows hyperintense lesions on T2WI located within the brainstem and dentate nuclei of the cerebellum[46]. It may also provide clue to the diagnosis of rarer infections like cryptococcal, fungal or amoebic affection of the brain. The severity of involvement detected on an MRI may also aid in prognostication. Proton magnetic resonance spectroscopy can produce specific peak-patterns in cases of abscess, such as the presence of lactate and cytosolic amino acids[47].

COMPARITIVE STUDIES

Bhalla A et al found that MRI was abnormal among 62.75% of the patients with AFE. Significant correlation was observed between MRI findings and the incidence of seizures. 50% of the patients with no focal neurological deficits also had found to be having abnormalities in MRI[48].

Yadav SS et al reported a case of a 3 year-old male child with low grade fever who was also a known case of febrile seizures. The seizures continued even after subsiding of fever and also upon addition of other anti epileptic agents. Day 4, they suggested MRI brain and found that there were diffuse symmetrical areas of restricted diffusion in bilateral cerebral hemispheres, involving mainly white matter. Adjacent cortices were also hyperintense. They conducted a followup MRI after 4 weeks and observed the resolution of lesions[49].

A study by Modi A et al observed the difference in pattern of MRI changes in AFE, based on the etiology. They found meningeal enhancement in 41% of patients with pyogenic meningitis. The bilateral T2 thalamic hyperintensities, in particular hemorrhage, was the most common finding seen in five patients of japanese encephalitis out of seven patients in whom MRI brain was done. MRI brain in two out of four patients of HSV encephalitis showed characteristic T2-weighted hyperintensity corresponding to edematous changes in the temporal lobes. In six patients, nonspecific MRI findings of meningeal enhancement with cerebritis and cerebral infarction were seen[50].

Takanashi J et al reported that although the pathophysiology behind the AFE among their recruited study population was unknown, their patients showed a distinctive encephalopathy syndrome and MRI was helpful in establishing the diagnosis of this encephalopathy. They found that the majority of the children were aged between 10 months to 4 years.

Clusters of complex partial seizures were a common type. MRI performed within 2 days of presentation showed no abnormality. Subcortical white matter lesions were observed on DWI between 3 and 9 days in all the recruited patients. T2-weighted images showed linear high intensity of subcortical U fibers in 13/17 patients. The lesions were predominantly frontal or frontoparietal in location with sparing of the perirolandic region. The diffusion abnormality disappeared between days 9 and 25 and cerebral atrophy was detected later than 2 weeks. Three patients having only frontal lesions had also relatively good clinical outcome[51].

MATERIALS AND METHODS

Source of data: Patients above the < 18 year old with the history of fever with disorientation with or without convulsion admitted at pediatric emergency of KLEs Dr.Prabhakar Kore Hospital and MRC, with diagnosis of sepsis during the 1 year period from January 2023 to December 2023.

Study design: Prospective, Observational- hospital-based study for one year

Study period: January 2023 to December 2023

Sample size: Based on the formula z2pq/d2, where p is the prevalence of the disease, p= (1-p); z is the constant which is 1.96; d is allowable error for the given study.

Prevalence of AFE in pediatric patients at our institute from June 2021 to June 22 was 1.5 to 2% of all the pediatric admissions and we would like to consider the allowable error of 5% for the present study. So, the expected sample size of our study was 30.11, approximately 30. We included 31 cases.

Inclusion criteria:

1. Patients of either gender aged less than 18-year-old visited the hospital with complaints of;
    - Fever with disorientation
    - Fever with convulsions
    - Even the cases of cerebral palsy with above conditions will also be included, to rule out secondary encephalopathy in such patients.
2. Parents of the children willing to give written informed consent to be part of study

Exclusion criteria:

1. History of trauma to head
2. Signs of sepsis
3. History of congenital bleeding disorders
4. History of implant in situ

After obtaining the ethical clearance, the patients were recruited based on the above-mentioned inclusion criteria. Written informed consent was taken after explaining to the parents about the complete protocol in their understandable language. Detailed history of the presenting complaints and other demographic data had been obtained by face-to-face interview. Below is the Modified Rankin Score used to analyze the encephalopathy based on symptomatology. (Modi A et al)[8]

Score	Description
0	No symptoms at all
1	No significant disability despite having symptoms; able to carry out All usual duties and activities.
2	Slight disability. Unable to carry out activities
3	Moderate disability. Requiring some help
4	Moderately severe disability. Unable to walk without assistance
5	Severe disability. Bedridden. Incontinent
6	Dead

All vital parameters such as Blood pressure, temperature, oxygen saturation and urine output will be monitored. ECG were done. GCS scale was assessed. Assessed for any lymph node involvement. Routine blood investigations such as Complete blood count (CBC), C reactive protein (CRP), Erythrocyte sedimentation rate (ESR), Renal function test (RFT), Liver function test (LFT), Chest X ray (CXR), urine routine/culture sensitivity (CS) and blood culture and sensitivity will be done. Cerebrospinal fluid (CSF) analysis had been done by lumbar puncture.

Also, the respective rapid or the serological tests had been done to find out probable viral and bacterial causes. Below are the diagnostic criteria used for different etiologies of acute febrile encephalopathy. (Modi A et al)[8]

RESULTS

Due to lack of time period for the recruiting cases and controls, their data collection we had included only the cases of febrile convulsions having brain changes on MRI. All these were analysed to look for the distribution of type of lesions.

Table 1: Distribution of age

Age	**N**	**%**
<1 year	6	19.4%
1 to 5.11 years	7	22.6%
6 to 10.11 years	7	22.6%
11 years and more	11	35.5%
Average age	9.85±2.7	
Minimum	10 days	
Maximum	17 years	

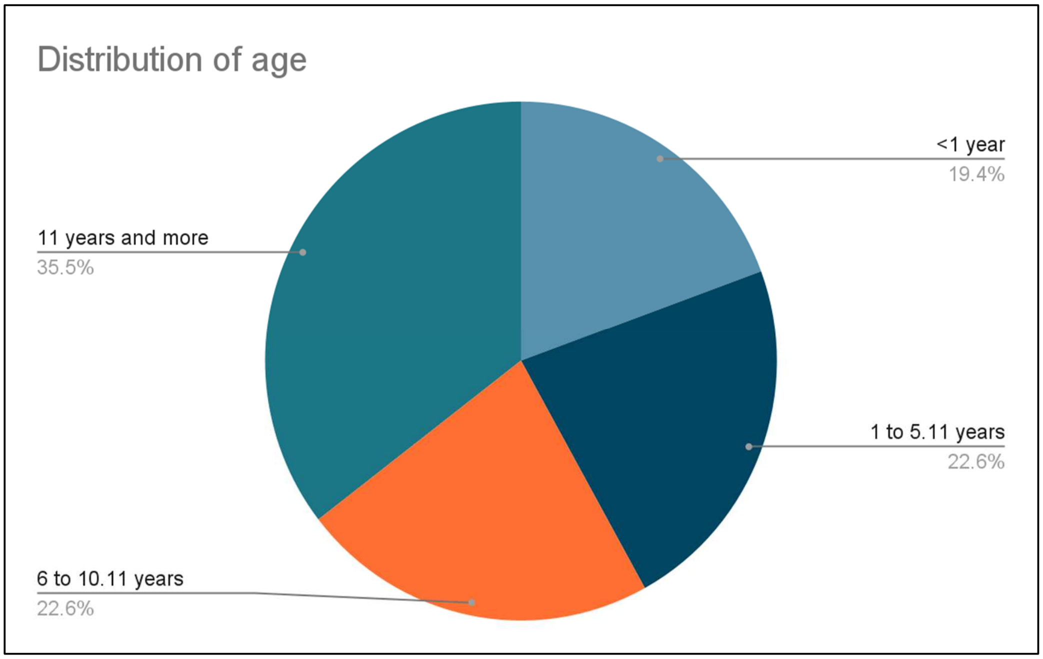

Figure 1: Distribution of age

The pattern of distribution of age amongst the study population is depicted in the chart above. The age group of above 11years had the maximum number of patients (11). While the age groups of 6 to 10.11 years and 1 to 5.11 years had 7 patients each. The age group of less than 1 year had the least number of patients (6).

Table 2: Distribution of gender

Gender	N	%
Male	14	45.2%
Female	17	54.8%

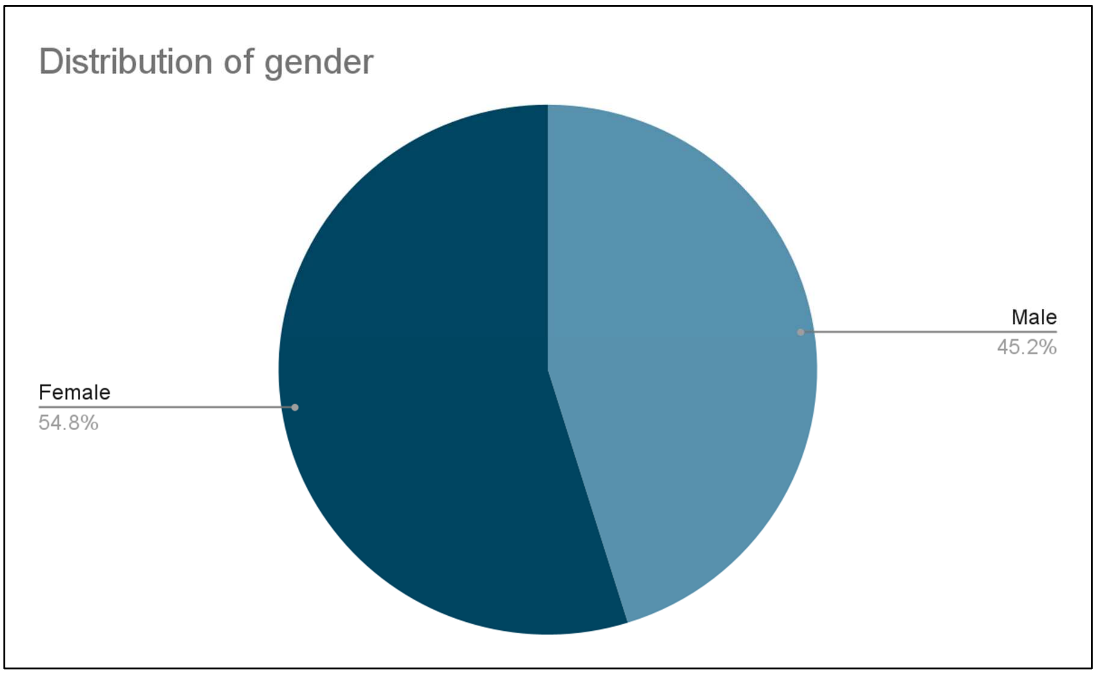

Figure 2: Distribution of gender

Out of the 31 participants, the majority were females i.e. 17(54.8%), while the rest of the 14 (45.2%) were males.

Table 3: Distribution of symptoms other than fever and convulsions

Symptom	N	%
Irritability	18	58.1%
Loose stools	11	35.5%
Excessive sleep	10	32.3%
Loss of consciousness	7	22.6%
Headache	7	22.6%
Burning micturation	5	16.1%
Lethargy	4	12.9%
Blurring of vision	2	6.5%
Cough	0	0.0%
Pain abdomen	0	0.0%

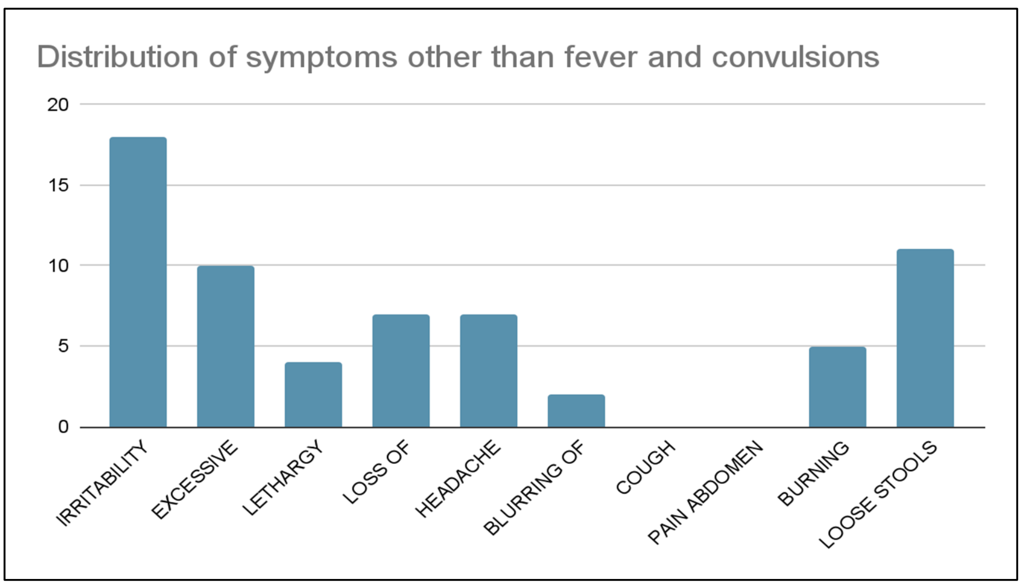

Figure 3:Distribution of symptoms other than fever and convulsions

Amongst our study population, apart from fever and convulsions, the most common symptoms was irritability in 18 (58.1%) patients followed by Loose stools in 11 (35.5%) patients and excessive sleep in 10 (32.3%) patients.

Table 4: Vital parameters

Parameter	**Mean or N**	**SD or %**
Average temperature	101	1.3
>100^0	21	67.7%
Average SBP	106	8.21
Average DBP	70	6.8
Average heart rate	110.16	10.54
HR >110	13	41.9%
Oxygen saturation <95%	Nil	

The average vital parameters of the study groupies depicted above. The average temperature of the patients was 101F with 21 of the patients having a temperature of 100F or above. The Average SBP was 106 while the the average DBP was 70 mm of hg in the study population. The average heart rate of the patients was 110.16bpm while 13 patients had a heart rate of 110 bpm or above. None of the patients had a saturation of less than 95%.

Table 5: Laboratory parameters

Parameter	**Values**	**Corresponding %**
Average WBC	7592±857.5 cells/ccmm	
Raise WBC	9	29%
Hypoglycaemia	2	6.5%

The average WBC count of the study population was 7592±857.5 cells/ccmm, while 9 of the patients had elevated WBC counts. Also, 2 of the patients had hypoglycemia.

Table 6: Distribution of MRI findings

Parameter	**N**	**%**
Bilateral periventricular and peritrigonal region	5	16.1%
Bilateral fronto-parieto-temporal region	2	6.5%
Right fronto-parieto-temporal region	2	6.5%
Bilateral basal ganglia, bilateral external capsule and bilateral thalami	1	3.2%
Bilateral caudate nuclei and bilateral putamenbilateral caudate nucleus, bilateral lentiform nucleus, bilateral thalami, bilateral uncus and pons	1	3.2%
Bilateral centrum semi ovale, bilateral corona radiata, posterior limb of internal capsule on right side, genu and splenium of corpus callosum, subcortical u fibers of fronto-parieto-temporal regions	1	3.2%
Bilateral fronto-parietal , left corona radiata and pons	1	3.2%
Bilateral fronto-parietal region	1	3.2%
Bilateral fronto-parieto-temporo-occipital region and bilateral	1	3.2%

globus pallidi		
Bilateral globus pallidi	1	3.2%
Bilateral hippocampus	1	3.2%
Bilateral internal capsule, splenium of corpus callosum, superior cerebral peduncles	1	3.2%
Bilateral medial temporal lobes and bilateral external capsule	1	3.2%
Bilateral occipital region	1	3.2%
Bilateral parietal region	1	3.2%
Bilateral periventricular and bilateral fronto-parietal region	1	3.2%
Bilateral thalamus, bilateral basal ganglia , bilateral caudate nucleus , bilateral cerebellum	1	3.2%
Bilateral thalamus, bilateral lentiform nucleus, splenium of corpus callosum, bilateral corona radiata , bilateral fronto-parietal region, dorsal brain stem	1	3.2%
Corpus callosum, bilateral cerebral peduncles and ventral brain stem	1	3.2%
Left medial temporal lobe, left parietal region	1	3.2%
Left medial temporal lobe, left posterior parietal and bilateral frontal regions	1	3.2%
Pons , bilateral thalami	1	3.2%
Right fronto-parieto-temporo-occipital region and left frontal region	1	3.2%
Splenium of corpus callosum	1	3.2%

The Bilateral periventricular and peritrigonal regions had the highest frequency of lesions in the study population i.e. in 5 (16.1%) of the patients

Table 7: Distribution of lesion appearance on T1 imaging

Parameter	N	%
Hypointense	28	90.3%
Isointense	3	9.7%

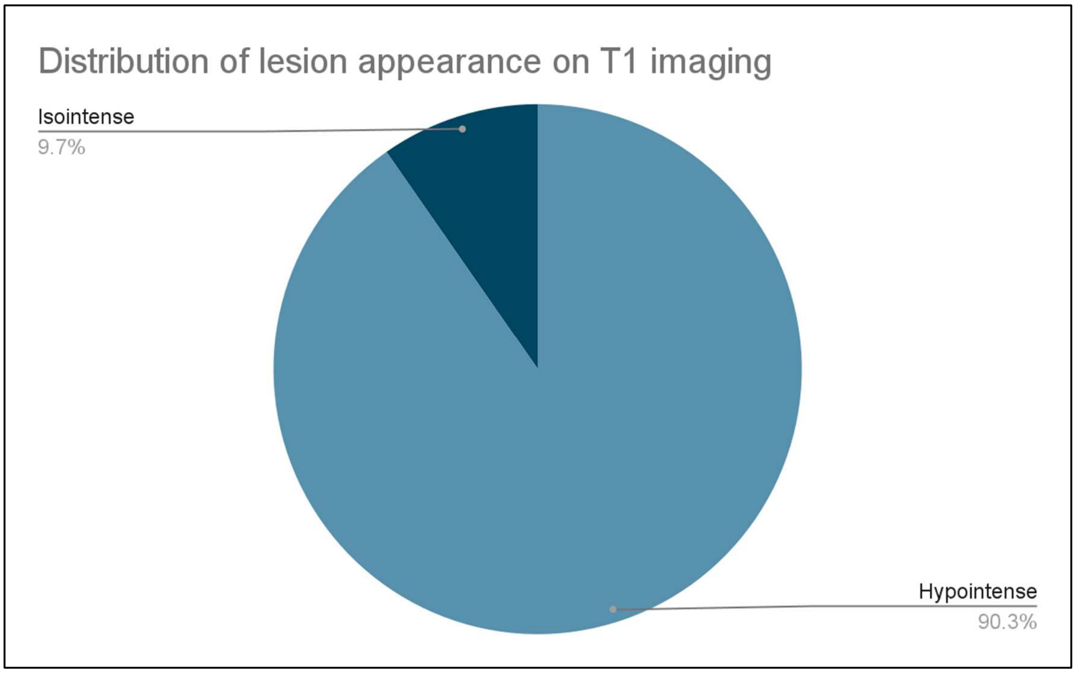

Figure 4:Distribution of lesion appearance on T1 imaging

In the majority of the patients in the study i.e 28 (90.3%) of the 31 patients had hypointense lesion on T1 imaging, while the rest of the 3(9.7%) patients had isointense lesions.

Table 8: Distribution of lesions on T2

Parameter	N	%
Hyperintense	29	93.5%
Isointense	2	6.5%

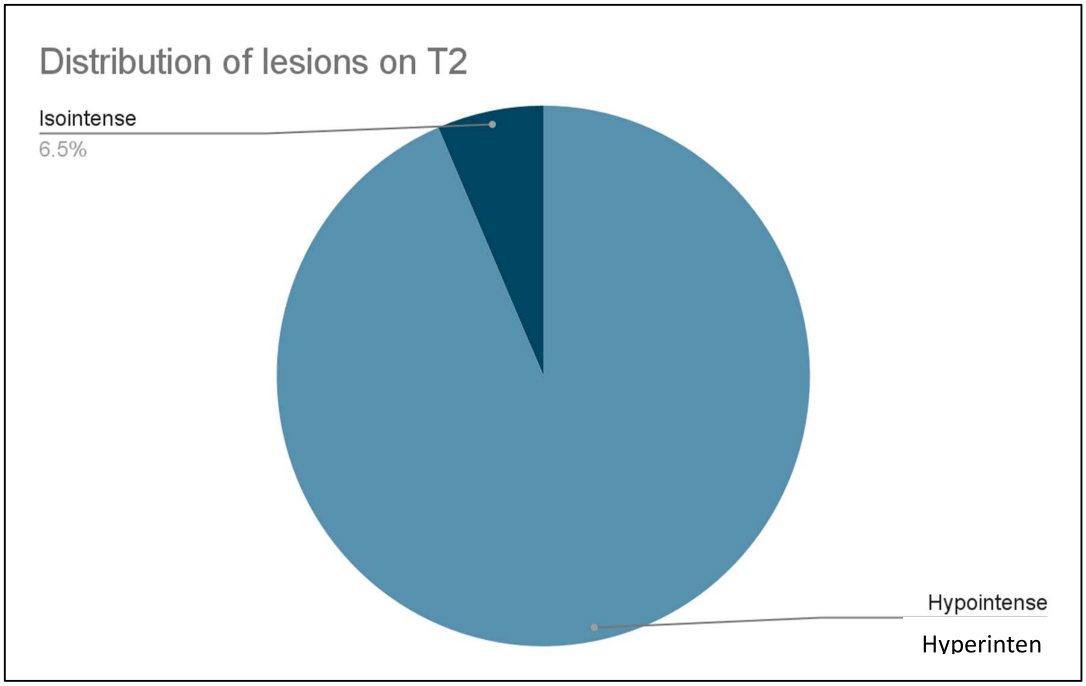

Figure 5: Distribution of lesions on T2

In the majority of the patients in the study i.e 29 (93.5%) of the 31 patients had hyperintense lesion on T2 imaging, while the rest of the (6.5%) patients had isointense lesions.

Table 9: Distribution of lesion appearance on flair MRI

Parameter	N	%
Hypointense	3	9.7%
Isointense	5	16.1%
Hyperintense	23	74.2%

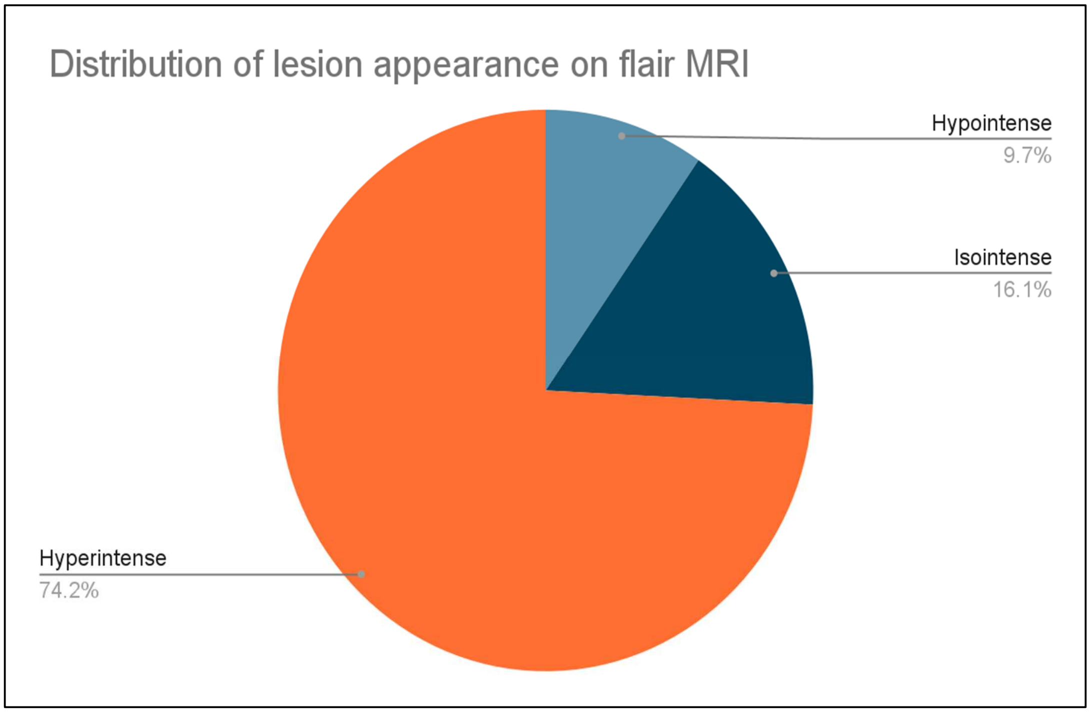

Figure 6: Distribution of lesion appearance on flair MRI

On the FLAIR sequence in MRI, majority of the lesions i.e. 23 (74.2%) appeared hyperintense. 5 (16.1%) appeared isointense while the remaining 3 (9.7%) of the lesions appeared hypointense.

Table 10: Distribution of diffusion restriction

Parameter	N	%
Restricting	24	77.4%
Not restricting	7	22.6%

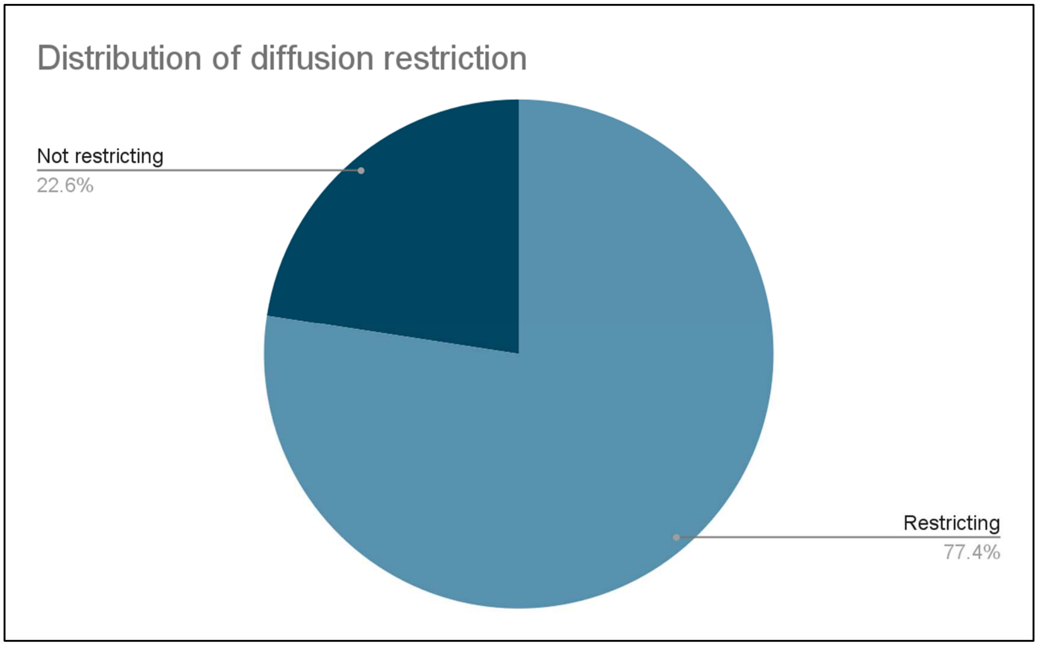

Figure 7: Distribution of diffusion restriction

Also, it was noted that the majority of the lesions i.e 24 (77.4%) had diffusion restriction on DWI sequence, while the remaining 7(22.6%) of the lesions did not have diffusion restriction on DWI sequencing.

Table 11: SWI distribution

Parameter	N	%
Blooming	5	16.1%
Not blooming	26	83.9%

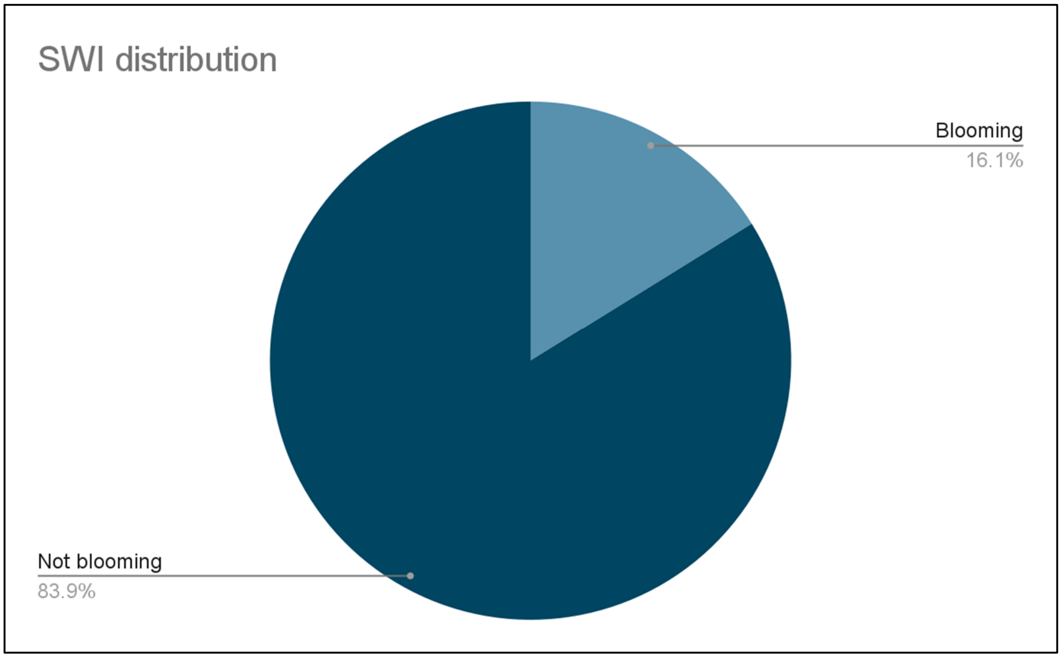

Figure 8: SWI distribution

26(83.9%) of the 31 lesions studied were not blooming on the SWI sequence while only 5 (16.1%) of the lesions had blooming.

Table 12: Final diagnosis

Diagnosis	N	%
Acute disseminated encephalomyelitis	2	6.5%
Acute encephalitis	3	9.7%
Acute hemorrhagic necrotizing encephalitis	2	6.5%
Cytotoxic lesion of corpus callosum	1	3.2%
Encephalitis	2	6.5%
Gliosis due to old vascular insult	2	6.5%
Herpes simplex virus encephalitis	2	6.5%
Ischemic encephalopathy	6	19.4%
Metabolic encephalopathy	2	6.5%
Post ictal edema	2	6.5%
Viral encephalitis	6	19.4%

The two most common diagnoses was ischaemic encephalopathy and viral encephalitis in 6(6.5%) of the patients each.

Table 13: MODIFIED RANKIN SCORE

Score	N	%
1	2	6.5%
2	14	45.2%
3	12	38.7%
4	3	9.7%

The majority of the patients had a modified Rankin score of 2 in 14(45.2%) of the patients or a score of 3 in 12 (38.7%) of the patients. Also, 3(9.7%) patients had a score of 4 and 2(6.5%) of the patients had a score of 1.

DISCUSSION

Out of 31 cases of febrile convulsions, all (100%) of our study population had one or the other changes observed on MRI. In our study, incidence of the children >/=11years was high accounting for about 11 (35.5%). Aged between 6 - 10.11 and 1 - 5.11 years had 7 (22.6%) patients each. <1 year were 6 (19.4%). The average age of our participants was 9.85±2.7. The lowest aged child was 10 days old and the highest being 17 years. Children aged <6 years were more than >6. There were 17(54.8%) of females and the rest 14 (45.2%) being male children. We did not find any difference in distribution of age and gender of our study group. Similarly, Das R et al[52] more were 25 males (69.44%) with Male to female ratio of 2.3:1. The mean age of presentation was 1.93 ± 0.85 years which was very lesser than the present clinical cases but they too had no significant distributional changes.

Amongst our study population, apart from fever and convulsions, the most common symptoms were. irritability amongst 18 (58.1%) cases, followed by Loose stools in 11 (35.5%) patients and excessive sleep in 10 (32.3%) affected population. Loss of consciousness, Headache, burning micturition, Lethargy and Blurring of vision were distributed among few of our patients. Blurring of vision incidence could of questionable as the children less than 6 might not be able to explain it better.

The mean temperature of the patients was $101F^0$ with 21 still having $>100^0$F on admission even after administering anti-pyretics. The Average SBP was 106±8.21, normal limit while the DBP was 70±6.8 mmHg. The average heart rate of the patients was 110.16±10.54bpm and 13(41.9%) had tachycardia. None of the patients had oxygen saturation <95%.

The average WBC count of the study population was 7592±857.5 cells/ccmm, while 9 of the patients had elevated than upper limit. Also, 2 of the patients had hypoglycaemia. Among these, lowered blood sugars might have further aggravated the convulsion. The bilateral periventricular and peri trigonal regions had the highest frequency of lesions in the study population i.e. in 5 (16.1%) of the patients. In most of the patients in the study i.e 28 (90.3%) of the 31 patients had hypointense lesion on T1 imaging, while the rest of the 3(9.7%) patients had isointense lesions. In the majority of the patients in the study i.e 29 (93.5%) of the 31 patients had hyperintense lesion on T2 imaging, while the rest of the (6.5%) patients had isointense lesions.

Unlike this study who reported 100% MRI changes, MRI lesions in Das R et al, changes were distinguished among 11 (30.56%) patients. Cortical focal hyperintensity (CFH) in 42.1% was the commonest.[52]In our cases, Bilateral periventricular and peritrigonal regionwas common, including 5 (16.1%) followed by 2 (6.5%) each with Bilateral fronto-parieto-temporal region and Right fronto-parieto-temporal region involvement.One each had Bilateral basal ganglia, bilateral external capsule and bilateral thalami, Bilateral caudate nuclei and bilateral putamenbilateral caudate nucleus, bilateral lentiform nucleus, bilateral thalami, bilateral uncus and pons, Bilateral centrum semi ovale, bilateral corona radiata, posterior limb of internal capsule on right side, genu and splenium of corpus callosum, subcortical U fibers of fronto-parieto-temporal regions, Bilateral fronto-parietal + left corona radiata and pons, Bilateral fronto-parietal region, Bilateral fronto-parieto-temporo-occipital region with bilateral globus pallidi, Bilateral globus pallidi, Bilateral hippocampus, Bilateral internal capsule+ splenium of corpus callosum + superior cerebral peduncles, Bilateral medial temporal lobes and bilateral external capsule, Bilateral occipital region, Bilateral parietal region, Bilateral periventricular + bilateral fronto-parietal region, Bilateral thalamus + bilateral basal ganglia + bilateral caudate nucleus + bilateral cerebellum, Bilateral thalamus + bilateral lentiform nucleus + splenium of corpus callosum + bilateral corona radiata + bilateral fronto-parietal region, dorsal brain stem, Corpus callosum + bilateral cerebral peduncles + ventral brain stem, Left medial temporal + parietal lobe, Left medial temporal lobe + left posterior parietal + bilateral frontal regions, Pons + bilateral thalami, Right fronto-parieto-temporo-occipital region and left frontal region, Splenium of corpus callosum.

The multiple seizures episode in 22 (61.11%) had significant association than single episodes which was 38.89% (14) in Das R et al.[52] In our study, T2 hyperintensity was found more and the unilateral lesions were common among our study population. Also, in Das R et al, MRI abnormality was cortical focal hyperintensity same as ours, among their cases, it was in 8 (42.10%) patients. 5(26.31%) had subcortical focal hyperintensity. Subcortical white matter abnormalities incidence was 3 (15.71%). Further, the frequency of focal cortical dysplasia in this study is 3 (15.71%). two (5.56%) had acute infarction of the right MCA territory, one (2.78%) had subacute infarction of the right frontal lobe, one (2.78%) had MRI features suggestive of tuberous sclerosis, one (2.78%) had early leukodystrophy changes, one (2.78%) patient had frontotemporal atrophy. However, one (2.78%) patient had acute disseminated encephalomyelitis (ADEM).[52,53]

Shinnar S et al observed that many of their patients had hyperintense lesions on T2 scan also unilateral hyperintensity was observed more than bilateral, which was the same as observed by Janszky J et al.[53,54]On the FLAIR sequence in MRI, majority of the lesions i.e. 23 (74.2%) appeared hyperintense. 5 (16.1%) appeared isointense while the remaining 3 (9.7%) of the lesions appeared hypointense. Also, it was noted that the majority of the lesions i.e 24 (77.4%) had diffusion restriction on DWI sequence, while the remaining 7(22.6%) of the lesions did not have diffusion restriction on DWI sequencing. 26(83.9%) of the 31 lesions studied were not blooming on the SWI sequence while only 5 (16.1%) of the lesions had blooming. The two most common diagnoses were ischaemic encephalopathy and viral encephalitis in 6(6.5%) of the patients each. The majority of the patients had a modified Rankin score of 2 among 14(45.2%) of the patients or a score of 3 in 12 (38.7%) of the patients. Also, 3(9.7%) patients had a score of 4 and 2(6.5%) of the patients had a score of 1.

Maytal J et al had a similar age distribution. Sapir D et al as well had more patients with multiple convulsion episodes.[55,56]Hesdorffer DC et al also had observed subcortical focal hyperintensity, abnormal white matter signals, and focal cortical dysplasia as commonest findings.[57] This could be explained by Shinnar S et al,[58] who interpreted that the presence of lesions in the brain would be reducing the threshold for development of convulsions. The same has been explained by Besson P et al and Alonso-Nanclares L et al.[59,60]

Other clinical studies by Kalnin AJ et al, Hesdorffer DC and Das S et al had reported the significant positive association between multiple focal convulsions and the brain lesions.[61,62]Das K et al and Das R et al had observed that the average duration of hospital stay of these patients with MRI changes was 7 days.[63,5]

CONCLUSION

Patients aged 11 years were more with male predominance but no positive association was observed in this distribution. 100% of the children with febrile convulsions had one or the other brain lesion. Involvement of Bilateral periventricular + peritrigonal region 5 (16.1%) followed by 2 (6.5%) each with Bilateral fronto-parieto-temporal region and Right fronto-parieto-temporal region involvement were the common sites affected. There was no association between the MRI changes and modified Rankin score.

SUMMARY

- Based on the available data, Acute febrile encephalopathy (AFE) in pediatric age group is one of the medical emergencies manifesting as of various systemic and CNS pathologies as well. As it shows wide deviation in clinical features and these being nonspecific, the diplomatic outcomes are observed. Also, the etiological spectrum is variable depending on the studied population by various research scholars. The changes in MRI would help us to analyse the associated functional abnormalities.
- The present study was taken to analyze the correlation between the severity of CNS signs, symptoms and the extent of lesions on MRI acute febrile encephalopathy in children and to analyze the variation in lesions found on MRI among different etiology of acute febrile encephalopathy in children.
- In this Prospective observational study for one year, the hospital-based study, we included 31 cases of acute febrile convulsion with disorientation having radiological changes but excluding the cases of head injury and not willing to be part of the study.
- In our study, the incidence of patients aged 11 years was higher, which was about 35.5% of the 31 cases included. Of 31 patients, 17(54.8%) were females and (45.2%) were males. Most common symptoms was irritability in 18 (58.1%) patients followed by Loose stools in 11 (35.5%). Viral encephalitis was the commonest diagnosis.
- Modified Rankin score of 2 in 14(45.2%) of the patients or a score of 3 in 12 (38.7%) of the patients. The outcome was better irrespective of the score. There was no association between the MRI changes and modified Rankin score and specific symptoms.

- Bilateral periventricular and peri trigonal region was the commonest MRI changes we observed with the incidence of about 16.1% (5/1). Bilateral fronto-parieto-temporal region and Right fronto-parieto-temporal region among two each. Rest were with wide distribution.

LIMITATIONS

LIMITATION OF OUR STUDY

We could not add the control group for analysis due to time constraint.

STRENGTH OF OUR STUDY

Of all the observed cases with changes in MRI, has been analysed for the commonest findings which would be one of the reliable pieces of evidence for the further clinical evaluations.

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ANNEXURES – I

INFORMED CONSENT FORM

INFORMATION ABOUT THE STUDY

Title of the clinical study: Prospective study on role of MRI in acute febrile encephalopathy in children

Study place: Department of Radio-diagnosis, JAWAHARLAL NEHRU Medical College, Belgaum

Details of the primary investigator

Name: REG. NO. BS0121008

Designation: POST GRADUATE (MD RADIO-DIAGNOSIS)

I, Dr. REG. NO. BS0121008, postgraduate, from the Department of Radio-diagnosis, JAWAHARLAL NEHRU Medical College, Belgaum, am carrying out a study on the topic, “Prospective study on role of MRI in acute febrile encephalopathy in children” with the objectives of analyzing the role of MRI in identifying the acute febrile encephalopathy in children.

The required details from you are the name, age, familial, previous and current medical history of the child in detail. The child will be monitored continuously till the time of discharge by the specialists.

The child will be subjected for laboratory investigations in order to find the cause of fever and the associated symptoms. After which the child will be subjected for MRI scan to rule out the involvement of brain and spinal tissue.

If you are uncomfortable, you have the right to withdraw from the interview / study at any time.

You will NOT be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone.

If you are willing to be part of this study, please read the following statement and give us the consent for further procedure.

CONSENT

The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s in the language I am comfortable with. Having understood the same, I hereby give my consent to them to interview me.

I, …………………………..am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements)

Signature/Thumb impression of the study participant	
Signature/Thumb impression of the witness Relationship with the patient	
Signature of the primary investigator	

ANNEXURE II-

PROFORMA

Name: Age: Gender: IP/OP number:

Presenting complaints:

Symptoms	Present	Absent	If present then Duration of illness	Number of episodes per day (If applicable)	History of contact with same symptoms (Applicable for epidemiological disease)
Fever					
Irritability					
Excessive sleep					
Lethargy					
Loss of consciousness					
Convulsions					
Headache					
Blurring of vision					
Cough					
Pain abdomen					
Burning micturition					
Loose stools					

VITALS

Vital	**Baseline**	**Follow up…..**				
BP						
Temperature						
Heart rate						
Oxygen saturation						

LABORATORY PARAMETERS

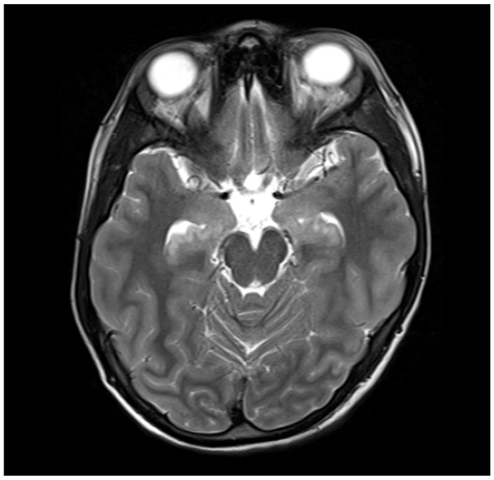
(Any significant changes will be noted down)

MRI findings:

Diagnosis:

ANNEXURE III:

FIGURES



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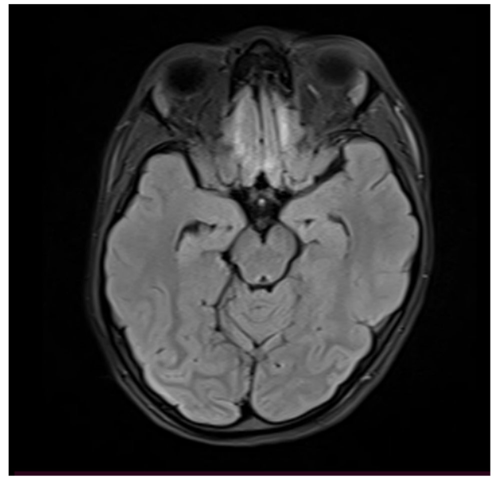

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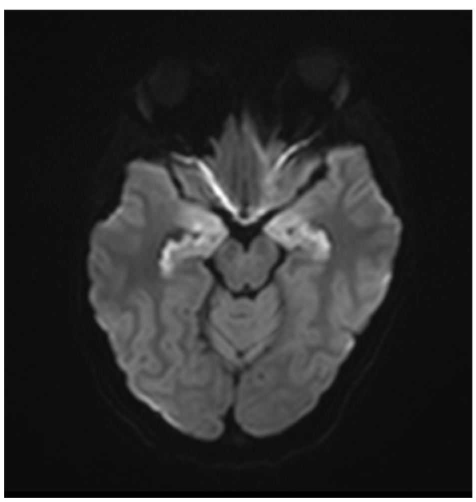

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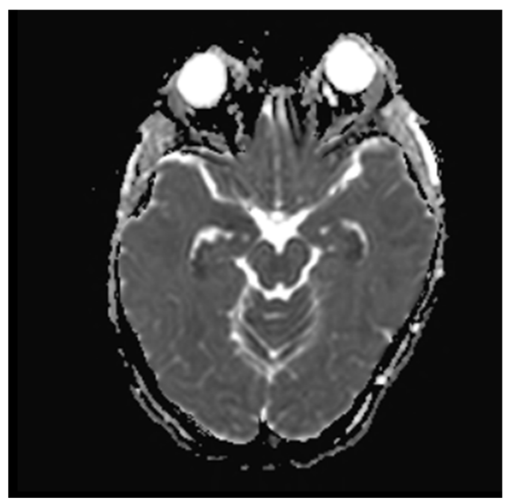
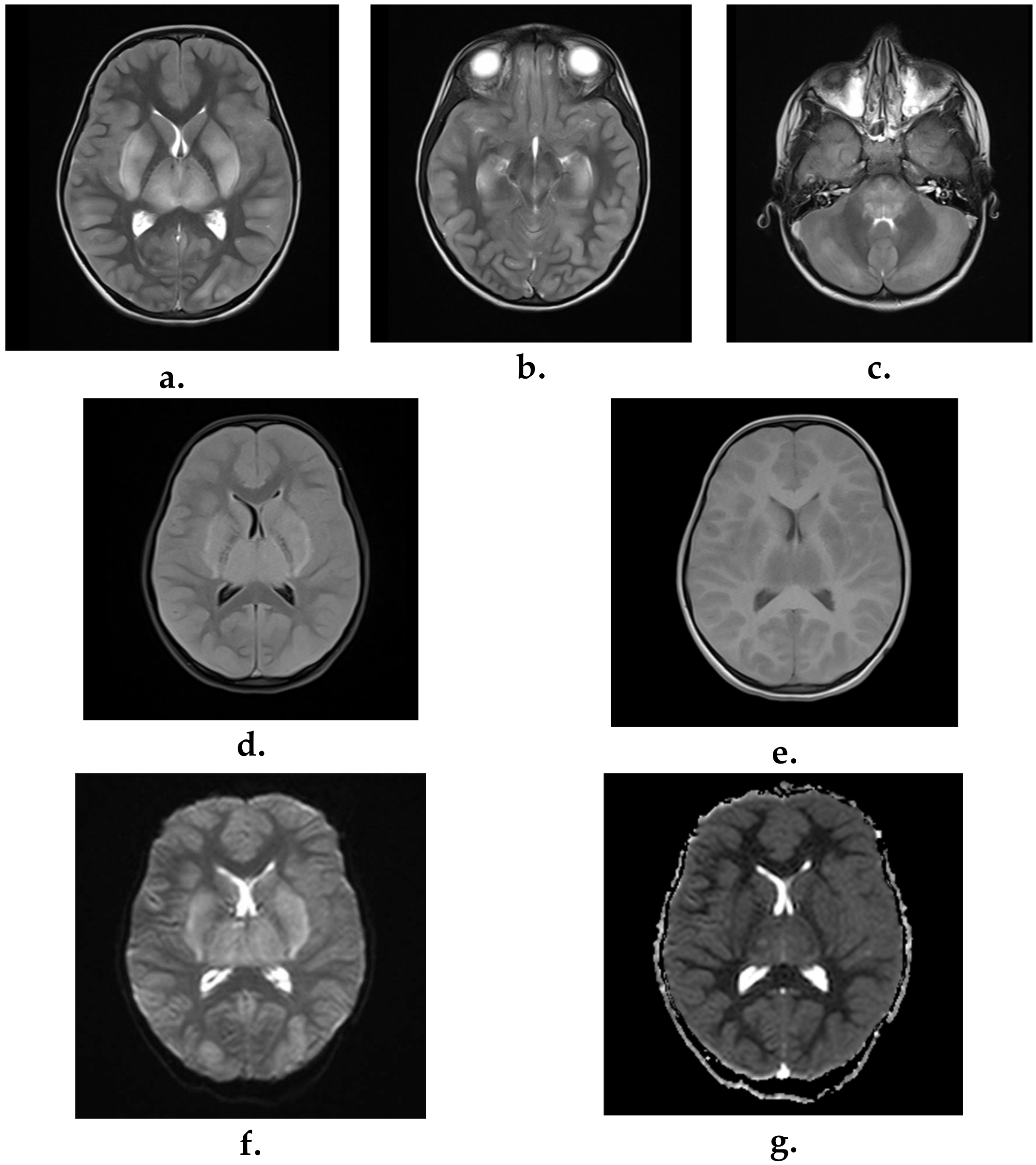


d.

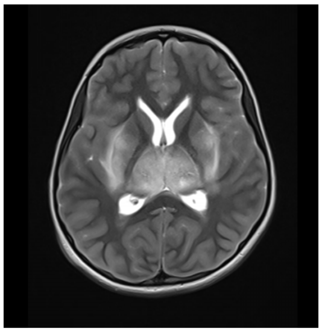
Bilateral symmetrical T2(a) hyperintense and FLAIR(b) isointense areas involving bilateral hippocampal region with evidence of diffusion restriction (c & d) in a case of viral encephalitis

CASE 2 (Figure 2)



T2 (a, b & c) & FLAIR (d) hyperintense areas and T1 (e) hypointense areas involving bilateral caudate nucleus, bilateral lentiform nucleus, bilateral thalami, uncus, bilateral parahippocampal gyrus and pons which shows restriction on DWI sequence (f & g) suggestive of acute encephalitis

CASE 3 (FIGURE 3)



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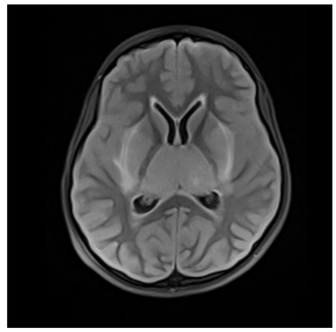

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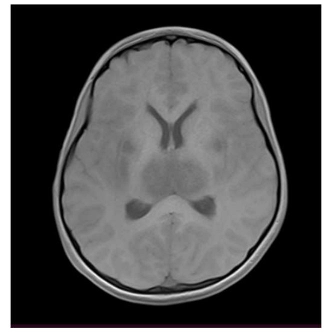

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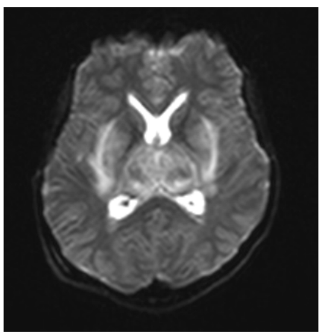
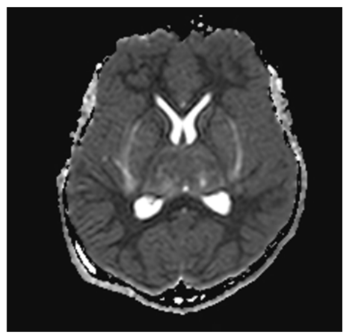
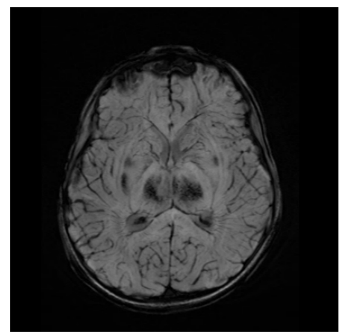


d.



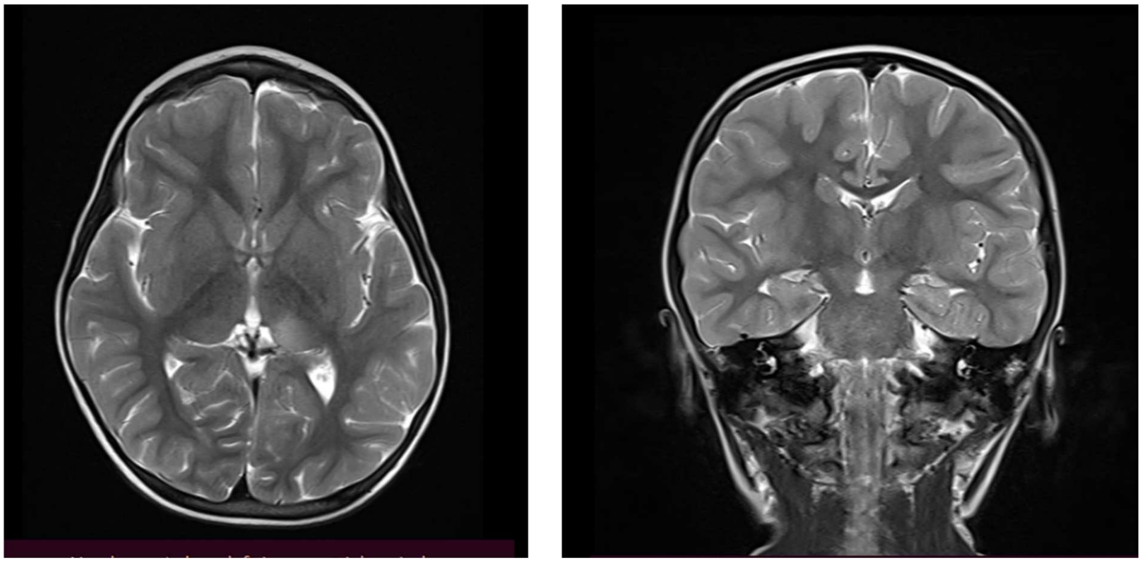
e.



f.

Symmetrical T2 (a) & FLAIR (b) hyperintense and T1 (c) hypointense areas involving bilateral basal ganglia, bilateral external capsule and bilateral thalami which shows diffusion restriction on DWI sequence (d & e) in bilateral thalami with blooming involving bilateral thalami & external capsule on SWI sequence (f) suggestive of acute hemorrhagic necrotizing encephalitis

CASE 4 (FIGURE 4)



a. b.

T2 hyperintense areas involving pons and bilateral thalami (left >right) with no evidence of diffusion restriction on DWI sequence and no evidence of blooming in SWI sequence suggestive of encephalitis

ANNEXURE – IV

KEY TO MASTER CHART

Fever	FE
Irritability	IR
Excessive sleep	ES
Lethargy	LE
Loss of consciousness	LO
Convulsion	CO
Headache	HA
Blurring of vision	BV
Cough	COU
Pain abdomen	PA
Burning micturation	BM
Loose stools	LS

Bilateral hippocampus	BH
Pons	PO
Bilateral thalami	BT
Bilateral medial temporal lobes	MT
Bilateral external capsule	EC

Bilateral fronto-parietal region	FP
Bilateral basal ganglia	BG
Bilateral caudate nucleus	CN
Bilateral cerebellum	CE
Bilateral periventricular & peritrigonal region	PP
Left medial temporal lobe	LMT
Left parietal region	LP
Right fronto-parieto-temporal region	RT
Right fronto-parieto-temporo-occipital region	RO
Bilateral lentiform nucleus	BLN
Bilateral uncus	BU
Bilateral putamen	BP
Bilateral internal capsule	IC
Splenium of corpus callosum	SCC
Superior cerebral peduncles	SCP
Bilateral frontal region	BF
Bilateral corona radiata	BC
Genu and splenium of corpus callosum,	GSC
Subcortical U fibers of fronto-parieto-temporal regions	SU

Master chart

SL NO	AGE	SEX	IP/OP NUMBER	FEVER	IRRITABILITY	EXCESSIVE SLEEP	LETHARGY	LOSS OF CONSCIOUSNESS	CONVULSION	HEADACHE	BLURRING OF VISION	COUGH	PAIN ABDOMEN	BURNING MICTURATION	LOOSE STOOLS	BP	TEMPERATURE	HEART RATE	OXYGEN SATURATION	LABORATORY PARAMETERS	AREAS OF BRAIN INVOLVED	T1	T2	FLAIR	DIFFUSION	SWI	DIAGNOSIS	MODIFIED RANKIN SCORE
1	14YRS	M	1170249	P	P	P	P	P	N	P	N	N	N	N	N	100/70	100	110	96	WBC-16000	BILATERAL HIPPOCAMPUS	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	VIRAL ENCEPHALITIS	1
2	4YRS	F	10019843	P	P	N	N	N	P	N	N	N	N	N	N	98/66	101	100	98	NORMAL	PONS , BILATERAL THALAMI	HYPOINTENSE	HYPERINTENSE	ISOINTENSE	NOT RESTRICTING	NO BLOOMING	ENCEPHALITIS	2
3	7YRS	F	10023150	P	P	N	N	P	P	P	N	N	N	N	N	96/70	99.9	98	96	WBC13000	BILATERAL MEDIAL TEMPORAL LOBES AND BILATERAL EXTERNAL CAPSULE	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	HERPES SIMPLEX VIRUS ENCEPHALITIS	2
4	9M	F	10025167	P	P	P	N	N	P	N	N	N	N	N	N	90/60	99.8	86	99	NORMAL	BILATERAL FRONTO-PARIETAL REGION	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	ACUTE DISSEMINATED ENCEPHALOMYLITIS	3
5	3YRS	M	10002528	P	P	N	N	N	P	N	N	N	N	N	N	100/68	102	130	98	NORMAL	BILATERAL THALAMUS, BILATERAL BASAL GANGLIA , BILATERAL CAUDATE NUCLEUS , BILATERAL CEREBELLUM	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	BLOOMING	ENCEPHALITIS	2
6	7YRS	M	7223381	P	P	N	N	N	P	N	N	N	N	N	N	98/68	100	140	96	NORMAL	BILATERAL PERIVENTRICULAR AND PERITRIGONAL REGION	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	ISCHEMIC ENCEPHALOPATHY	3
7	5YRS	M	1185379	P	P	N	N	N	P	N	N	N	N	N	N	100/60	101	96	97	WBC-14500	LEFT MEDIAL TEMPORAL LOBE, LEFT PARIETAL REGION	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	BLOOMING	HERPES SIMPLEX VIRUS ENCEPHALITIS	3
8	3YRS	M	1200593	P	P	N	N	P	P	N	N	N	N	N	N	90/68	99.9	106	96	NORMAL	RIGHT FRONTO-PARIETO-TEMPORAL REGION	HYPOINTENSE	HYPERINTENSE	ISOINTENSE	RESTRICTING	NO BLOOMING	POST ICTAL EDEMA	2
9	2YRS	F	1206805	P	P	N	N	N	P	N	N	N	N	N	N	90/60	103	150	99	WBC-15300	RIGHT FRONTO-PARIETO-TEMPORO-OCCIPITAL REGION AND LEFT FRONTAL REGION	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	VIRAL ENCEPHALITIS	2
10	7YRS	F	260585	P	P	P	N	N	P	P	N	N	N	N	N	100/70	102	116	98	WBC-12800	BILATERAL CAUDATE NUCLEUS, BILATERAL LENTIFORM NUCLEUS, BILATERAL THALAMI, BILATERAL UNCUS AND PONS	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	ACUTE ENCEPHALITIS	3
11	4M	F	255014	P	N	N	N	N	P	N	N	N	N	N	N	90/60	100	168	95	NORMAL	BILATERAL PARIETAL REGION	HYPOINTENSE	HYPERINTENSE	HYPOINTENSE	NOT RESTRICTING	NO BLOOMING	ISCHEMIC ENCEPHALOPATHY	3
12	9YRS	F	1006624	P	P	N	N	P	P	N	N	N	N	N	N	100/68	101	130	92	WBC-15700	BILATERAL BASAL GANGLIA, BILATERAL EXTERNAL CAPSULE AND BILATERAL THALAMI	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	BLOOMING	CUTE HEMORRHAGIC NECROTIZING ENCEPHALITI	4
13	15YRS	M	1009463	P	N	N	N	N	P	N	N	N	N	N	N	116/76	100	80	94	NORMAL	BILATERAL FRONTO-PARIETO-TEMPORAL REGION	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	VIRAL ENCEPHALITIS	2
14	10YRS	F	10019854	P	P	P	N	N	P	N	N	N	N	N	N	100/66	99.9	125	98	NORMAL	BILATERAL FRONTO-PARIETAL , LEFT CORONA RADIATA AND PONS	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	NOT RESTRICTING	NO BLOOMING	ACUTE DISSEMINATED ENCEPHALOMYLITIS	3
15	5YRS	M	10025579	P	P	N	N	N	P	N	N	N	N	N	N	90/62	99.8	88	97	WBC-13700	BILATERAL THALAMUS, BILATERAL LENTIFORM NUCLEUS, SPLENIUM OF CORPUS CALLOSUM, BILATERAL CORONA RADIATA , BILATERAL FRONTO-PARIETAL REGION, DORSAL BRAIN STEM	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	BLOOMING	CUTE HEMORRHAGIC NECROTIZING ENCEPHALITI	4
16	7YRS	M	238118	P	P	P	N	N	P	N	N	N	N	N	N	98/66	100	90	96	NORMAL	BILATERAL FRONTO-PARIETO-TEMPORO-OCCIPITAL REGION AND BILATERAL GLOBUS PALLIDI	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	VIRAL ENCEPHALITIS	2

SL NO	AGE	SEX	IP/OP NUMBER	FEVER	IRRITABILITY	EXCESSIVE SLEEP	LETHARGY	LOSS OF CONSCIOUSNESS	CONVULSION	HEADACHE	BLURRING OF VISION	COUGH	PAIN ABDOMEN	BURNING MICTURATION	LOOSE STOOLS	BP	TEMPERATURE	HEART RATE	OXYGEN SATURATION	LABORATORY PARAMETERS	AREAS OF BRAIN INVOLVED	T1	T2	FLAIR	DIFFUSION	SWI	DIAGNOSIS	MODIFIED RANKIN SCORE
17	13YRS	F	11929059	P	N	N	N	N	P	N	N	N	N	N	N	100/60	101	104	98	NORMAL	BILATERAL PERIVENTRICULAR AND PERITRIGONAL REGION	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	NOT RESTRICTING	NO BLOOMING	ISCHEMIC ENCEPHALOPATHY	3
18	17YRS	M	11889340	P	P	P	N	N	P	N	N	N	N	N	N	110/78	99.9	124	99	WBC-12680	BILATERAL CENTRUM SEMI OVALE, BILATERAL CORONA RADIATA, POSTERIOR LIMB OF INTERNAL CAPSULE ON RIGHT SIDE, GENU AND SPLENIUM OF CORPUS CALLOSUM, SUBCORTICAL U FIBERS OF FRONTO-PARIETO-TEMPORAL REGIONS	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	BLOOMING	CUTE HEMORRHAGIC NECROTIZING ENCEPHALITI	4
19	7YRS	M	6965238	P	N	N	N	N	P	N	N	N	N	N	N	100/66	100	100	95	NORMAL	BILATERAL PERIVENTRICULAR AND PERITRIGONAL REGION	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	NOT RESTRICTING	NO BLOOMING	ISCHEMIC ENCEPHALOPATHY	3
20	16YRS	F	10008178	P	N	P	P	P	P	P	N	N	N	P	P	108/74	101	76	96	WBC-13450	LEFT MEDIAL TEMPORAL LOBE, LEFT POSTERIOR PARIETAL AND BILATERAL FRONTAL REGIONS	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	ACUTE ENCEPHALITIS	2
21	12YRS	M	236661	P	N	N	N	P	P	P	N	N	N	P	P	98/66	99.8	90	98	NORMAL	BILATERAL PERIVENTRICULAR AND PERITRIGONAL REGION	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	POST ICTAL EDEMA	2
22	15YRS	M	10005315	P	N	N	P	P	P	P	N	N	N	N	N	110/80	99.9	98	97	BLOOD SUGAR-78	BILATERAL CAUDATE NUCLEI AND BILATERAL PUTAMEN	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	METABOLIC ENCEPHALOPATHY	3
23	10DAYS	F	11928067	P	P	P	P	N	P	N	N	N	N	N	P	90/60	100	166	98	BLOOD SUGAR-64	BILATERAL INTERNAL CAPSULE, SPLENIUM OF CORPUS CALLOSUM, SUPERIOR CEREBRAL PEDUNCLES	ISOINTENSE	ISOINTENSE	ISOINTENSE	RESTRICTING	NO BLOOMING	METABOLIC ENCEPHALOPATHY	3
24	12YRS	M	10005064	P	N	N	N	N	P	P	P	N	N	P	P	100/66	100	94	99	NORMAL	BILATERAL PERIVENTRICULAR AND PERITRIGONAL REGION	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	ACUTE ENCEPHALITIS	2
25	5 MONTHS	F	10005678	P	P	P	N	N	P	N	N	N	N	N	P	90/66	101	120	95	NORMAL	BILATERAL FRONTO-PARIETO-TEMPORAL REGION	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	VIRAL ENCEPHALITIS	2
26	17YRS	F	1163407	P	N	N	N	N	P	N	N	N	N	N	P	110/70	102	78	97	NORMAL	SPLENIUM OF CORPUS CALLOSUM	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	CYTOTOXIC LESION OF CORPUS CALLOSUM	3
27	14YRS	M	1178906	P	N	N	N	N	P	N	P	N	N	N	P	100/64	101	90	98	NORMAL	RIGHT FRONTO-PARIETO-TEMPORAL REGION	HYPOINTENSE	HYPERINTENSE	HYPOINTENSE	NOT RESTRICTING	NO BLOOMING	GLIOSIS DUE TO OLD VASCULAR INSULT	1
28	5YRS	M	244316	P	N	N	N	N	P	N	N	N	N	P	P	100/60	100	88	96	NORMAL	BILATERAL OCCIPITAL REGION	HYPOINTENSE	HYPERINTENSE	HYPOINTENSE	NOT RESTRICTING	NO BLOOMING	GLIOSIS DUE TO OLD VASCULAR INSULT	2
29	1MONTH	M	255678	P	P	P	N	N	P	N	N	N	N	N	P	90/60	99.8	130	96	NORMAL	CORPUS CALLOSUM, BILATERAL CEREBRAL PEDUNCLES AND VENTRAL BRAIN STEM	ISOINTENSE	ISOINTENSE	ISOINTENSE	RESTRICTING	NO BLOOMING	ISCHEMIC ENCEPHALOPATHY	2
30	17YRS	F	233678	P	N	N	N	N	P	N	N	N	N	P	P	110/70	99.9	100	97	NORMAL	BILATERAL PERIVENTRICULAR AND BILATERAL FRONTO-PARIETAL REGION	HYPOINTENSE	HYPERINTENSE	HYPERINTENSE	RESTRICTING	NO BLOOMING	ISCHEMIC ENCEPHALOPATHY	3
31	10 MONTHS	M	1187897	P	N	N	N	N	P	N	N	N	N	N	P	88/66	100	144	99	NORMAL	BILATERAL GLOBUS PALLIDI	ISOINTENSE	HYPERINTENSE	ISOINTENSE	RESTRICTING	NO BLOOMING	VIRAL ENCEPHALITIS	2