YIELD OF MAGNETIC RESONANCE IMAGING WITH SPECTROSCOPY IN CHILDREN WITH NEW ONSET AFEBRILE SEIZURE BETWEEN ONE MONTH TO TWENTY-FOUR MONTHS OF AGE

BY

REGISTRATION NO. BS0117004

Dissertation

Submitted to the

KLE Academy of Higher Education and Research, Belagavi, Karnataka

In partial fulfillment

of the requirements for the degree of

M.D.
IN
RADIO-DIAGNOSIS

DEPARTMENT OF RADIO-DIAGNOSIS,
J. N. MEDICAL COLLEGE,
BELAGAVI -590010. KARNATAKA

APRIL 2020

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH, BELAGAVI, KARNATAKA

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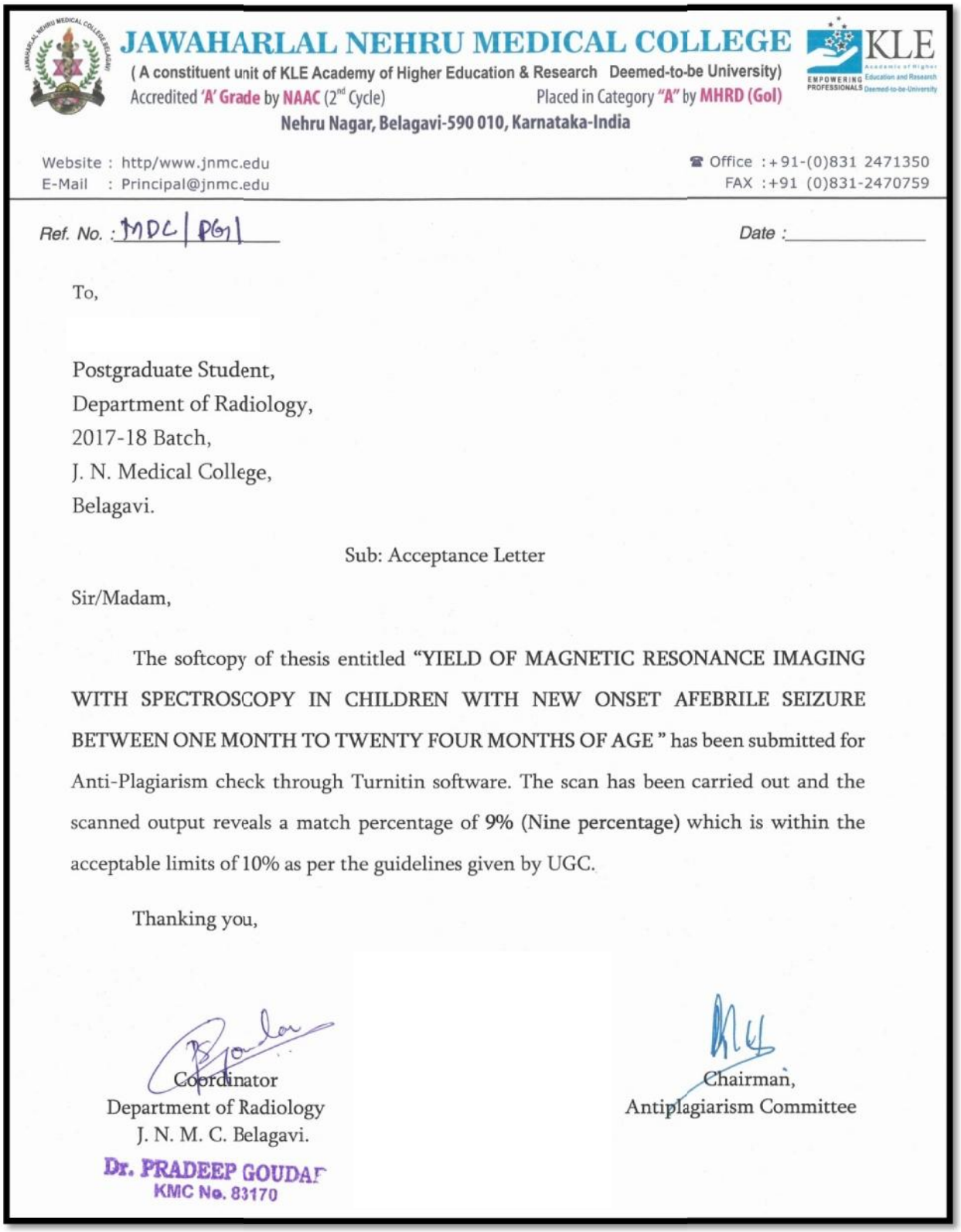

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LIST OF ABBREVIATIONS

3D	:	Three dimension
3D MPRAGE	:	3D magnetization prepared rapid acquisition gradient echo
3D SPGR	:	3D spoiled gradient recalled echo
ADC	:	Apparent diffusion coefficient
CISS	:	Constructive interference in steady state
CSE	:	Conventional spin echo
CSF	:	Cerebrospinal fluid
CT	:	Computed tomography
DWI	:	Diffusion weighted imaging
EEG	:	Electro encephalogram
FLAIR	:	Fluid attenuated inversion recovery
fMRI	:	Functional MRI
FSE	:	Fast spin echo
Gd	:	Gadolinium
GE	:	Gradient echo
GTCS	:	Generalized tonic clonic seizures
HIV	:	Human immunodeficiency virus
ILAE	:	International league against epilepsy
IR	:	Inversion recovery
MCD	:	Malformations of cortical development
MRA	:	MR angiogram
MRI	:	Magnetic resonance imaging
MRS	:	Magnetic resonance spectroscopy
NAA	:	N-acetyl aspartate
NCC	:	Neurocysticercosis
NMR	:	Nuclear magnetic resonance
PC	:	Phase contrast
RF	:	Radio frequency
SOL	:	Space occupying lesions
STIR	:	Short Tau inversion recovery
T	:	Telsa
T1WI	:	T1 weighted image
TLE	:	Temporal lobe epilepsy
TOF	:	Time of flight
TR	:	Repetition time
WHO	:	World Health Organization

ABSTRACT

Background & objectives

A seizure is “an abnormal high burst of synchronized neuronal activity affecting neuronal networks resulting in clinical manifestations that are sudden, brief, and usually transient”.

Magnetic Resonance Imaging (MRI) is the present choice of imaging in patients who present with seizures. MRI identifies structural lesions that require prompt response from the treating physicians such as high-grade gliomas, arteriovenous malformations, infections and malformations of cortical development.

Proton (1H) magnetic resonance spectroscopy (MRS) is an MR modality that measures CNS metabolites.MRS can be used with MRI in the assessment of children with seizures. MRI is commonly regarded as a tool for the assessment of new onset seizures.

There is a need to study the role of neuroimaging in the new onset seizures in the age group of 1-24 months as it gives a higher positive study as compared to the older children age group and also affects the treatment protocol and leads to better outcome. American academy of neurology recommends non urgent neuroimaging like magnetic resonance imaging in a new onset seizure in the age group of 1-24 months.

The objectives of this study are to establish to study the presenting features of first-onset afebrile seizures in children (age 1–24 months) and the yield of neuroimaging, to collect indications which are necessary to make

recommendations for the use of routine MRI in children (age 1- 24 months) with first onset afebrile seizures and to detect structural anomalies in the brain that may be related to the cause of seizures with supplementation of MR spectroscopy.

Materials and methods

One year hospital based observational study was done in Department of Radio-diagnosis at the KLE'S Dr. Prabhakar Kore hospital & MRC, Belagavi.

31 patents were included in the study. These patients are subjected to Magnetic resonance imaging with proton spectroscopy to detect the underlying pathological and structural anomalies causing first onset seizures.

Distribution according to Age and sex, on the basis of duration of seizures, on MR diagnosis, percentage of abnormal MR diagnosis and abnormalities in various age groups were calculated.

Results

Maximum number of patients (41.94 %) were in the group of 0-6 months of age. Ratio of Male: female was almost equal (51.61: 48.39 %). Out of 31, 16 were male and 15 were female. Most of the children presented with seizures of 2-minute duration.

In 12 out of 31 children (38.70 %), the study was normal and 19 (61.29 %) patients showed magnetic resonance imaging abnormalities. In 19 abnormal patients, 11 were male (57.90%) and 8 were female (42.10 %). In 4 children (12.90 %) structural malformations was noted. 4 children showed imaging

abnormalities which were due to inborn metabolic errors. Imaging abnormalities were noted maximum in the children between 0-6 months of age.

Interpretation and conclusion

Precise diagnosis of the cause of seizure is vital for finding an effective treatment. MRI has been shown to be highly sensitive and specific in recognizing the underlying pathology in seizures. With its high spatial resolution, excellent inherent soft tissue contrast, multiplanar imaging capability and lack of ionizing radiation, MR imaging has emerged as a resourceful tool in the evaluation of patients with seizures.

Routine use of magnetic resonance imaging after first onset seizures helps to identify the underlying pathophysiological causes and its severity and thus helping in further medical and surgical management.

As per our study, use of MRI with spectroscopy resulted in early detection of the structural malformations, inborn metabolic errors, infectious causes and also other various causes resulting in prompt definitive treatment.

These results suggest that Use of MRI with spectroscopy can be used as a routine screening tool for assessment of the new onset seizures in the neonatal life.

Studies with a larger sample size with immediate and long-term follow-up is required to include routine MRI screening as a modality after new onset seizure.

Future studies could compare the use of MRI and EEG for better diagnosis of the pathophysiology thus resulting in prompt accurate treatment protocol.

Keywords: Magnetic resonance imaging, Spectroscopy and Seizures.

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INTRODUCTION

A seizure is "an abnormal high burst of synchronized neuronal activity affecting neuronal networks resulting in clinical manifestations that are sudden, brief, and usually transient."[1]

First-onset seizures are the common type of neurologic emergencies happening during neonatal period, with approximately 4-10% of children / year presenting with newly occurring seizure disorders due to diverse etiologies.[2] New onset childhood seizures tend to happen most common in infancy (1–24 months) with a decreasing incidence through the rest of childhood.[3]

Magnetic Resonance Imaging (MRI) is the present choice of imaging in patients who present with seizures[4]. MRI identifies structural lesions that require prompt response from the treating physicians such as high-grade gliomas, arteriovenous malformations, infections and malformations of cortical development.[5]

Approximately, half of imaging studies in new-onset seizures were found to be abnormal.15-20% of imaging provided etiological information and 2-4% provided causes that altered medical management leading to prompt care.[6,7,8,9]

Proton (1H) magnetic resonance spectroscopy (MRS) is an MR modality that measures CNS metabolites. MRS can be used with MRI in the assessment of children with seizures.[10] MRI is commonly regarded as a tool for the assessment of new onset seizures.[3,11,12]

MRI is included in the "The International League Against Epilepsy (ILAE)"standards for the assessment of epilepsy in 2009 and in its references for the management of infantile seizures again in 2015.[13,14]

MRS however, is not widely used for the assessment of many types seizures in children and thus has not been incorporated in the ILAE guidelines.[13,14]

The multiple MR sequences makes it possible for greater sensitivity and specificity for the detection of intra and extra axial processes. MR imaging is also the only imaging modality which can distinguish the myelination process in the neonatal brain.

Supplementation of MR spectroscopy with MRI sequences helps in differentiating structural lesions, developmental malformations, in born errors of metabolisms.

Neonatal MR imaging is fast becoming essential in predicting neuro-developmental outcomes, and the future of MR imaging is mainly aimed at understanding the prognosis and its implications of the CNS disease in newborn.

There is a need to study the role of neuroimaging in the new onset seizures in the age group of 1-24 months as it gives a higher positive study as compared to the older children age group and also affects the treatment protocol and leads to better outcome. American academy of neurology recommends non urgent neuroimaging like magnetic resonance imaging in a new onset seizure in the age group of 1-24 months.

AIMS & OBJECTIVES

1. To study the presenting features of first-onset afebrile seizures in children (age 1–24 months) and the yield of neuroimaging.
2. To collect indications which are necessary to make recommendations for the use of routine MRI in children (age 1- 24 months) with first onset afebrile seizures.
3. To detect structural anomalies in the brain that may be related to the cause of seizures with supplementation of MR spectroscopy.
4. To study the diverse etiological factors for seizures.
5. To find out the common imaging abnormality in patients with seizures.

REVIEW OF LITERATURE

HISTORICAL REVIEW

MRI as a neuroimaging modality has developed as a main clinical stay over the past 30 years. The roots of MRI can be tracked back for over a century and was previously known as NMR.[15]

NMR concept was first proposed by the Dutch physicist C-J Gorter in 1936. Modern clinical use of NMR was first suggested by Paul Lauterbur's (1973) to use magnetic field gradient to encode position dependent information in the NMR signal.

The history of nuclear MR started with fundamental studies which were presented in 1938, when Isid or Isaac Rabi guided a ray of molecules through a magnetic field and confirmed that radio waves are emitted at specific frequencies. He was granted the 1944 Nobel Prize in Physics.[16]

Paul Lauterbur showed in 1973 that we could use nuclear MR to generate an image[17].

Lauterbur and Sir Peter Mansfield were conferred the joint 2003 Nobel Prize in Physiology or Medicine in acknowledgement of their extra ordinary efforts. First human MR images were published in 1977, 6 years post the first human CT images. The first human MR imaging, centered on the field focused nuclear MR (FONAR) voxel-imaging method, took nearly 5 hours to be produced.

MR spectroscopy is a non-invasive test which analyses the amount of biochemicals in brain and thus detecting abnormal increase or decrease of certain chemicals in particular pathologic conditions.

There are many clinically available varieties of techniques of MR spectroscopy including single voxel and multi voxel chemical shift imaging which are routinely used to grade malignant lesions and also used to differentiate between infective and neoplastic etiologies. Recent advances also include the use of MR spectroscopy in grading of prostatic carcinomas.

MR spectroscopy has been routinely used in recent times in pediatric population to differentiate the cause of neonatal seizures including inborn errors of metabolism, cortical dysplasias and neoplastic etiologies.

Purcell et al[18] and Bloch et al [19] elucidated the principles of nuclear magnetic resonance in1946. In 1951, Proctor and Yu[20] suggested that the resonance frequency of a nucleus hinges on its chemical structure, which creates a small, but perceptible, variation in the Larmor resonance frequency of that nucleus. This nuclear component is termed “chemical shift”.

Protons (1H) have been commonly used for MR spectroscopy because of their high natural copiousness in organic assemblies and high nuclear magnetic sensitivity paralleled with any other magnetic nuclei [21].

Phosphorus 31 MR spectroscopy has also been in use clinically to study variations in high energy metabolism in a number of diseases.

ANATOMY

The human brain is one of the most complicated organs in the body. For interpretation of the neuro-imaging, knowledge about the brain development and basic anatomy is vital.

Brain Development:

Human brain development begins from the third gestational starting week with the differentiation of the neural progenitor cells. Neural progenitor cells are arranged in a cranio caudal fashion in the upper layer of the three-layered embryo. The neural plate contains the cells meant for differentiation into nervous tissue. This neural plate is located along the mid dorsal region in front of the primitive pit. The lateral folds of the neural elevate and form the two neural folds. These neural folds approach the midline, invaginate and form the neural tube[22].

Neural tube is the first major well-defined structure to be formed in the central nervous system. Neural tube is formed after about 20 days.

The rostral portion of the neural tube develops into the three vesical dilatations at the end of 3rd week differentiating into the forebrain (prosencephalon), midbrain (mesencephalon), & hindbrain (rhombencephalon).

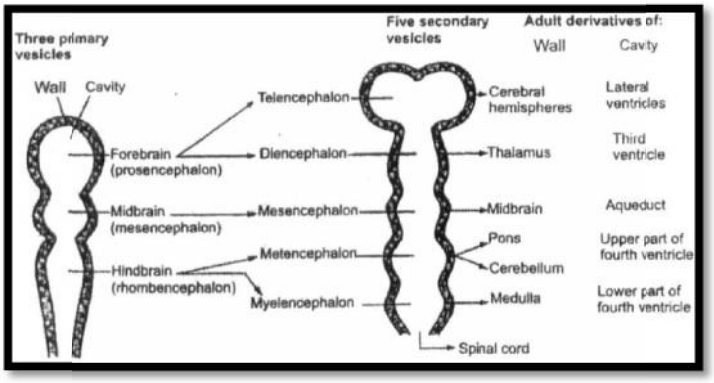


Fig. 1 :"Diagrammatic sketches of the brain vesicles indicating the adult derivatives of their walls and cavities"

The developing brain divides into a cephalic telencephalon and a caudal diencephalon by the end of fifth week of gestation. The hind brain subdivides into the metencephalon and myelencephalon. The metencephalon further divides into the adult pons and cerebellum and myelencephalon divides into the adult medulla[23].

Telencephalon divides into the two diverticula which later form the adult cerebral hemispheres. By the fourth month, these hemispheres undergo complex expansion and folding and form the permanent primitive fissures by the fourth month. Three major flexures, the midbrain, pontine and cervical flexures divide the developing brain into the cerebrum, cerebellum and spinalcord.

The human brain begins as a smooth, "lissencephalic" structure and gradual development of the characteristic pattern gyral and sulcal folding is noted. There is orderly sequential formation of the gyri and sulci by the end of sixth and seventh month of gestation[24].

The neuron production is seen around the period of mid gestation. The pool of primitive neuroprogenitor cells line along the lateral ventricles which proliferate and migrate outward to the cortex in an "inside out" sequence, and mature as neural and glial cells. During the sixth and seventh fetal months adult pattern of primitive gyri and sulci by the end of gestation.

Gross Anatomy:

Brain lies in the intracranial cavity and is composed of cerebrum, cerebellum and brain stem. The cerebrum is a paired neural structure which develops from the telencephalon and is composed of the two lateral cerebral hemispheres (left and right).

The brain is covered by three meningeal layers, namely duramater, arachnoid and piamater. The brain can be discussed under three major headings and is divided into the forebrain, mid brain and hind brain.

The forebrain is subdivided into the lateral cerebral hemispheres. The hind brain is further subdivided into the cerebellum, medulla oblongata and pons[24].

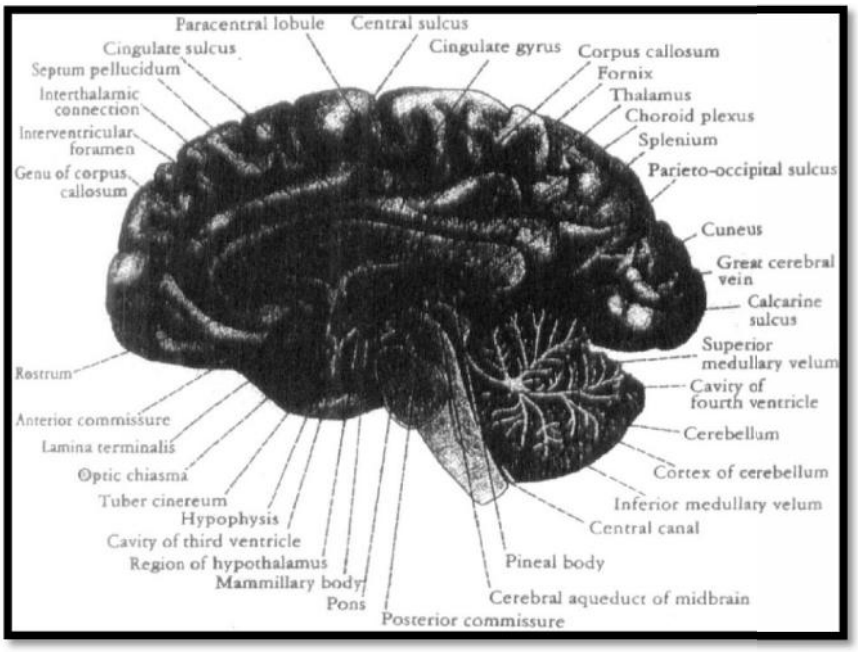


FIG.2 "MEDIAN SAGITTAL SECTION OF THE BRAIN TO SHOW GROSS ANATOMY"

Forebrain:

1. ***Diencephalon***: consists of dorsal thalamus and a ventral hypothalamus and is not seen from the external surface of the bran. Thalamus is the larger of the two and contains symmetrical egg-shaped masses and lie lateral to the third ventricle. Hypothalamus is situated inferior to the thalamus as the name suggests and lies in close correlation with the pituitary gland and bilateral limbic systems.

2. ***Cerebrum***: The two lateral cerebral hemispheres form the largest part of the brain and the two are connected by a white matter mass called corpus callosum. The cerebral hemispheres are connected to the brain stem via the cerebral peduncles. The two hemispheres enclose the two lateral ventricles which contain the cerebrospinal fluid. The hemispheres are separated by cleft called longitudinal fissure which projects into the falx cerebri. The cortex consists of multiple gyri and sulci. Gyri are the folds in the cortex with the fissures called as sulci. The hemispheres are subdivided into the lobes by the multiple prominent sulci. These lobes are given names based on the bones of skull which lie above them.

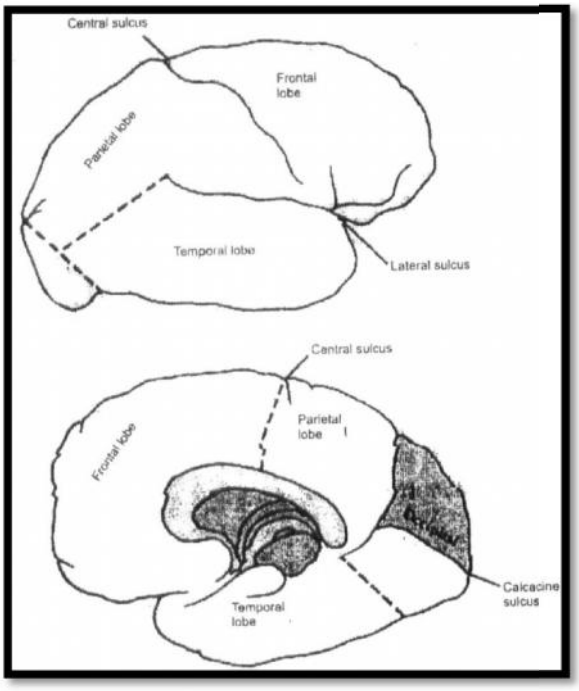


FIG.3: A & B: "LATERAL AND MEDIAL VIEWS OF THE RIGHT CEREBRAL HEMISPHERE SHOWING THE LOBES"

The cerebral hemispheres contain the central deep white matter and multiple deep grey white matter nuclei called basal ganglia. Basal ganglia contain caudate nucleus, lentiform nucleus and subthalamic nuclei and substantia nigra. Corona radiata are a pair of white matter tracts which are seen at the level of lateral ventricles. Corona radiata is group of nerve fibres which are arranged like a fan. It converges into the basal ganglia inferiorly and superiorly into the centrum semiovale. Corona radiata passes inferiorly as the internal capsule. Medial to the internal capsule lies a nucleus called caudate nucleus. Head of the caudate nucleus lies lateral to the frontal horn of lateral ventricles and the body of caudate nucleus lies beside the lateral ventricles. Lentiform nucleus is situated adjacent to the internal capsule and consists the putamen and globus pallidus in its anterosuperior and posteroinferior part respectively.

Midbrain

It lies between the hindbrain and forebrain. It contains many nuclei and bundles of ascending and descending nerve fibers.

Hindbrain:

1. ***Medulla Oblongata***: Connects the pons to the spinal cord. Many nuclei are situated in it and it serves as a conduit for ascending and descending nerve fibers.

2. ***Pons***: Is situated just in front of the cerebellum, below the midbrain and above the medulla oblongata. It also comprises of many nuclei, ascending and descending nerve fibers.

3. ***Cerebellum:*** Is situated posterior to the pons and the medulla oblongata in the posterior cranial fossa. It consists of two hemispheres connected by the vermis. The cerebellum is connected to the midbrain by superior cerebellar peduncles, to the pons by the middle cerebellar peduncles, and to the medulla by the inferior cerebellar peduncles. Certain masses of gray matter are embedded in white matter, the largest of these is known as the dentate nucleus[25].

Ventricular System:

Ventricles are the spaces located within the brain containing the cerebrospinal fluid (CSF) and the choroid plexus. There are two lateral ventricles positioned inside the cerebral hemispheres. The lateral ventricles communicate with the third ventricle through the foramina of Monro. Third ventricle lies in between the two thalami and is linked to the fourth ventricle via the "cerebral aqueduct". The fourth ventricle is present posterior to the pons and medulla and anterior to the cerebellum. It communicates with the subarachnoid space through the three foramina proximally and continues distally with the central canal of spinal cord[25].

Choroid plexus is specialized structure which has the function of secreting CSF. CSF flows through the ventricular system and also in the subarachnoid spaces supporting the central nervous system. CSF is absorbed into the superior sagittal sinus primarily through the arachnoid villi[25].

CLINICAL ASPECTS

CLASSIFICATION:

The commonly used classification of seizures is ILAE predominantly based on "clinical seizure type" and "interictal EEG findings".[26]

I. Partial seizures (Localization related)

- A) Simple partial seizures (consciousness not impaired)
  1. With motor signs (including Jacksonian versive and postural)
  2. With somatosensory or special sensory symptoms
  3. With autonomic symptoms
  4. With psychic symptoms
  5. With mixed symptoms
- B) Complex partial seizures (consciousness impaired)
  1. Simple partial onset followed by impaired consciousness.
  2. With impaired consciousness at onset
  3. With automatisms.
- C) Partial seizures with secondarily generalized

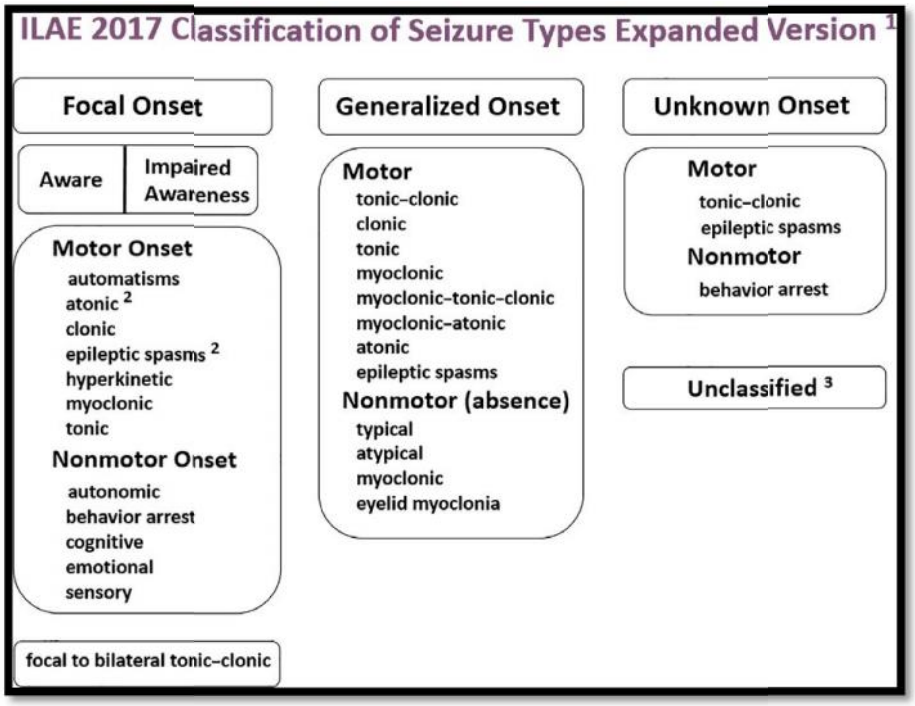
II. Generalized seizures of non focal origin(convulsive or non convulsive)

- A) Absence seizures
  1. With impaired consciousness only (Petit mal)
  2. With one or more of the following components : Atonic, Tonic and Autonomic and automatisms
- B) Myoclonic seizures
- C) Tonic seizures
- D) Tonic-clonic seizurs
- E) Atonic seizures

III. Unclassified epileptic seizures

INTERNATIONAL LEAGUE AGAINST EPILEPSY CLASSIFICATION OF EPILEPTIC SEIZURES (1981)

ILAE 2017 CLASSIFICATION OF SEIZURE TYPES EXPANDED VERSION



MRI has brought about significant changes in neuroimaging and is one of the recommended methods to evaluate the structure of the brain without invasive techniques.

The MRI findings in a patient with seizure disorders may be extremely variable. The variation can range from a normal scan to one showing a lesion indicated by altered signal intensity in different sequences.

The accuracy of MR in determining the substrate category in intractable epilepsy has been reported to be 88%.

For temporal lobe epilepsy (complex partial seizures) MR sensitivity of 75% to 100%, for hippocampal sclerosis greater than 90%, for other focal lesions including tumors has been reported based on histopathological findings as the gold standard.

The sensitivity of MR for detecting epileptogenic abnormalities in children undergoing epilepsy surgery has been found to be 75% or higher.

Causes of seizures:

Neonates (<1month)	:	Perinatal hypoxia and ischemia
		Intracranial hemorrhage and trauma
		Acute CNS infections
		Metabolic disturbances
		Drug withdrawal
		Developmental disorders
		Genetic disorders
Infants and children (>1 month to <12years):		Febrile seizures
		Genetic disorders
		CNS infections
		Developmental disorders Trauma

Pathophysiology:

The pathophysiology of epilepsy is diverse and cannot be explained by a single mechanism which is satisfactory for the different types and categories of the seizures.

Seizures occur as a result of shift in the normal balance of excitation and inhibition within the central nervous system.

Seizures are the end product of a state of increased neuronal excitability with or without synchronization. Any change in normal neuronal circuit excitability because of increased inherent excitability, increased recurrent excitation, with or without deficient recurrent inhibition are the main reasons that are required for seizure activity to occur. In other words, a slight enhancement or reduction of normal cerebro-cortical function could induce a seizure.[27]

There are certain provocative or precipitating factors that induce seizures in patients with epilepsy. Similarly, precipitating factors are responsible for causing the single seizure in someone without epilepsy. Precipitants include those due to intrinsic psychological or physical stress, sleep deprivation or hormonal changes associated with menstrual cycle. They also include exogenous factors such as exposure to toxic substances and certain medication.

Basic mechanisms of the seizures:

1. Initiation of seizures and propagation: Mechanism of seizures can be divided into initiation of the seizures in a particular region of cortex and propagation of the seizures where the seizures are propagated to the other regions of the brain.

2. The initiation phase is characterized by two concurrent events in an aggregate of neurons:

a. High frequency bursts of action potentials

b. Hypersynchronisation.

The bursting activity is caused by a long-lasting depolarization of the neuronal membrane due to influx of extracellular calcium (Ca^{2+}), which leads to the opening of voltage dependent sodium (Na^{+}) channels with its influx thus leading to the generation of repetitive action potentials. This is followed by a hyperpolarizing after potential mediated by GABA receptors or potassium (K^{+}) channels, depending on the cell type.

The spread of bursting activity is normally prevented by hyperpolarization and a region of adjacent inhibition which is created by inhibitory neurons. With adequate activation there is participation of surrounding neurons via few different mechanisms. Repetitive discharge leads to the following.

1. An increase in extracellular K^{+} which blunts hyper polarization and depolarizes neighboring neurons.
2. Accumulation of calcium in presynaptic terminals, leading to enhanced neuro transmitter release.
3. Depolarization induced activation of N-methyl-D-aspartate (NMDA) subtype of excitatory amino acid receptor, which causes calcium influx and neuronal activation. The recruitment of a sufficient number of neurons leads to a loss of the surrounding inhibition and propagation of seizure activity into contiguous areas via local cortical connections, and to more distant areas via long commissural pathways.[28]

The causes of epilepsy can be categorized into genetic and acquired disorders. Some genetic causes can affect in structural changes that are easily identifiable by cross-sectional imaging.

The causes of acquired epilepsy includes a broad category of abnormalities, such as vascular, neoplastic, traumatic, post-infective and metabolic causes. MRI is generally done to define the underlying pathological event, be it structural or owing to changes in the local chemical environment, such as edema or gliosis.

A large number of eminent personnel have worked on the role of MRI in assessment of patients with seizures or epilepsy.

D.T. Hsieh. et al, studied 317 infants presenting with new onset seizures found over half the infants to have imaging abnormalities which potentially altered medical management.[29]

CEREBRAL DYSGENESIS:

Cerebral dysgenesis is a spectrum of brain development disorders and includes

1. Dysgenesis of corpus callosum,
2. Malformations of cortical development

Dysgenesis of Corpus callosum: It refers to the defective development of the corpus callosum which is a midline structure. It can be partial or complete. If it is complete then the more appropriate term of agenesis is used. Dysgenesis of the corpus callosum can be primary or secondary.[30]

Corpus callosum usually develops from 12^{th} to 20^{th} week of gestation. The development starts anteriorly and then proceeds posteriorly. It starts from the genu and which starts around 12^{th} week. Rostrum is the last part to be formed around 20^{th} week. Based on the time of intrauterine result on the placenta, there might be complete agenesis or partial agenesis of the corpus callosum. If the insult occurs before 12^{th} week, there will be complete agenesis of the corpus callosum. Presence of the rostrum of the corpus callosum usually rules out the corpus callosal anomalies[31].

Corpus callosal anomalies can be detected during antenatal sonographic evaluation with lesser sensitivity and specificity[32].

Cross sectional imaging has been the modality of choice for detecting corpus callosal anomalies.

MR Imaging findings:

1. Bilateral lateral ventricles run parallel to each other as opposed to the normal lateral ventricles which have a bow tie appearance.

2. On coronal sections, the "high-riding" third ventricle looks as if it opens directly into the interhemispheric fissure. There is a thin membranous roof which actually bulges into the interhemispheric fissure, thus displacing the fornices laterally.

3. Non-crossing of the Probst bundles. Probst bundles are the white matter bundles which are supposed to cross the mid line through the corpus callosum but instead run lateral parallel to the interhemispheric fissures due to dysgenesis of the corpus callosum.

4. On diffusion tensor imaging, prominent green tracts of the Probst bundles are seen.[33]

Malformations of cortical development: Malformations of cortical development are usually identified as pathological sources of epilepsy and neuro developmental deficits in infants[34]. MRI significantly exhibits the abnormalities in more detail. Neuroimaging Commission of the ILAE, categorizes malformations as follows.

1. Diffuse cortical malformations: agyria, pachygyria, polymicrogyria, microcephaly, megalencephaly,microdysgenesis.
2. Focal or multifocal cortical malformations: focal cortical dysplasia, hemimegalencephaly, focal polymicrogyria, tuberoussclerosis,
3. Heterotopias.[35]

Other, more detailed classification of MCDs into four basic categories as follows

Classification:

- Abnormal neuronal and glial proliferation
- Abnormal neuronal migration
- Abnormal cortical organization
- Unclassified miscellaneous group.[36]

Focal cortical dysplasia is among the most common causes of epilepsy attributable to focal cerebral dysgenesis. 60% FCD is found in temporal lobes.[37]

MRI findings in patients with FCD include the following:

- Cortical thickening observed on atleast 3 or more contiguous slices.
- Blurring of the gray-white matter junction
- Increased signal of the underlying white matter on T2-weighted image/FLAIR.
- Often, a linear, curvilinear, or funnel-shaped tapering of abnormal signal intensity extending from the cortical white matter junction to the ependymal surface of the lateral ventricle[38].
- A deep or wide sulcus, with thickened gray matter at the depth of a sulcus.
- Broadening of agyrus[39].

Polymicrogyria: It is a malformation due to an alteration of the cortical development in the late stage of neuronal migration[40]. The deeper layers of the cortex form multiple small gyri with derangements of normal sulcation. It may be unilateral or bilateral. It is characterized by

- Numerous small gyri.
- Predilection for sylvian fissure.
- Atrophy mainly posteriorly
- Anomalous venous drainage.[41]

METHODOLOGY

Patients in the age group of 1-24 months with new onset seizures presenting to Child Development Centre and Department of Radio-Diagnosis at the KLE'S Dr. Prabhakar Kore hospital & MRC, Belgaum.

Method of collection of data:

1. **Source of Data:** KLE's Dr. Prabhakar Kore Hospital and Medical research center, Belagavi
2. **Study design:** Hospital based Observational study
3. **Sample size:** Prevalence of new onset seizures in age group of 1-24 months in Indian population in most of the studies done very less (less than 1 %).Therefore, all cases with new onset seizures in age group of 1-24 months evaluated on magnetic resonance imaging during the study period will be the sample size.
4. **Sampling method:** Universal sampling

All patients will be evaluated clinically and then undergo an MRI of the brain performed using a 1.5 Tesla MRI scanner (Magnetom Avanto TIM, 18 channel; Siemens, Erlangen, Germany) and 3.0 Tesla MRI scanner (Magnetom Spectra, 32 channel; Siemens, Erlangen, Germany) within seven days from the onset of seizures. Routine spin echo T1, T2 and Inversion recovery sequences are followed by a T1 weighted high resolution magnetization prepared rapid gradient echo sequence (MPRAGE), Magnetic resonance spectroscopy (MR spectroscopy), Susceptibility weighted imaging and a high-resolution inversion

recovery (IR) sequence both obtained in an oblique coronal plane perpendicular to the hippocampus.

DURATION:One year – between January 2018 to December 2018

(a) **Inclusion criteria:**

1. Patients with new onset of afebrile seizures within 1-24 months of age.
2. Patients with consent to participate in the study

3. Exclusion criteria:

1. Any previously diagnosed non central nervous system disorders liable to cause seizures.
2. Patients with known contraindications to MRI.
3. Syncopal and hypoglycemic attacks, pseudo-seizures or drug induced seizures.
4. Patients presenting with head injury/meningitis/encephalitis.
5. Parents/ Guardians who do not give consent

(c) Proposed method of Statistical data analysis:

1. Descriptive Statistics

MRI SEQUENCES THAT WILL BE OBTAINED:

1. T1 weighted image
2. T2 weighted image
3. FLAIR image
4. T1 inversion image
5. Magnetization Prepared Rapid Acquisition GRE (MP RAGE)
6. Proton Density Image
7. Multi voxel MR spectroscopy if MRI is normal/ focal lesion is present
8. Susceptibility Weighted Imaging

RESULTS

Table -1 : AGE AND SEX WISE DISTRIBUTION

AGE (MONTHS)	Male	Female	Total	Percentage
1 - 6	6	7	13	41.94
7 - 12	4	5	9	29.03
13 - 18	3	1	4	12.9
19 - 24	3	2	5	16.13
Total	16 (51.61%)	15 (48.39%)	31	100.00

Maximum number of patients (41.94 %) were in the group of 1-6 months of age.

Ratio of Male: female was almost equal (51.61: 48.39 %).

Out of 31, 16 were male and 15 were female.

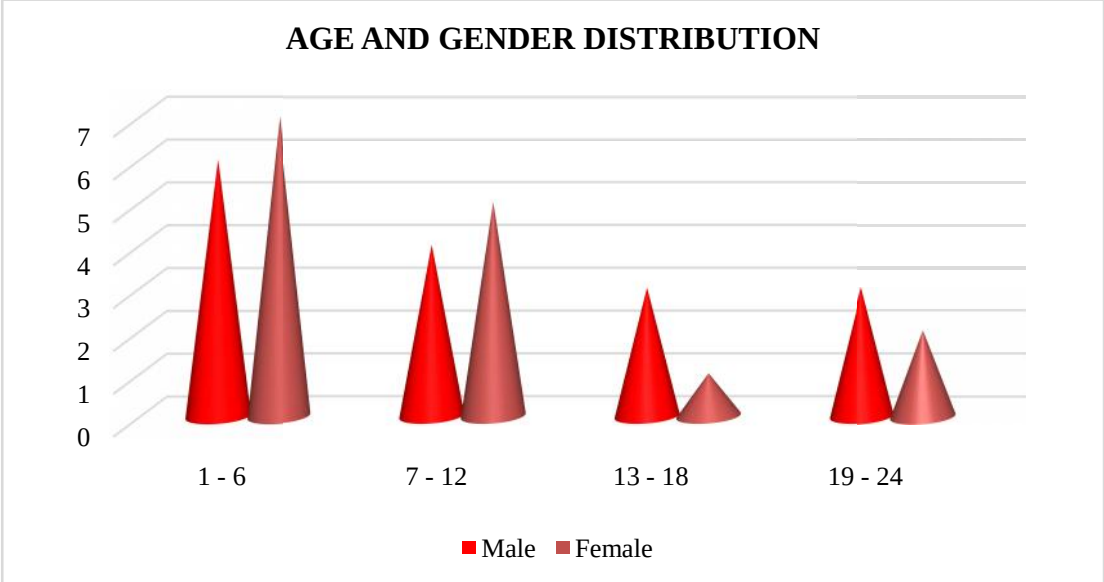


TABLE -2 DISTRIBUTIONS OF PATIENTS ON THE BASIS OF CLINICAL DIAGNOSIS OF SEIZURES.

Types of seizures	Generalized onset	Focal onset	Unknown onset	Focal to generalized onset
Number of patients	5	22	3	1

Maximum number of patients (71.0 %) presented with seizures of focal onset, 16 % presented with seizures with generalized onset. 10% presented with seizures with unknown onset and 3 % presented with focal to generalized onset.

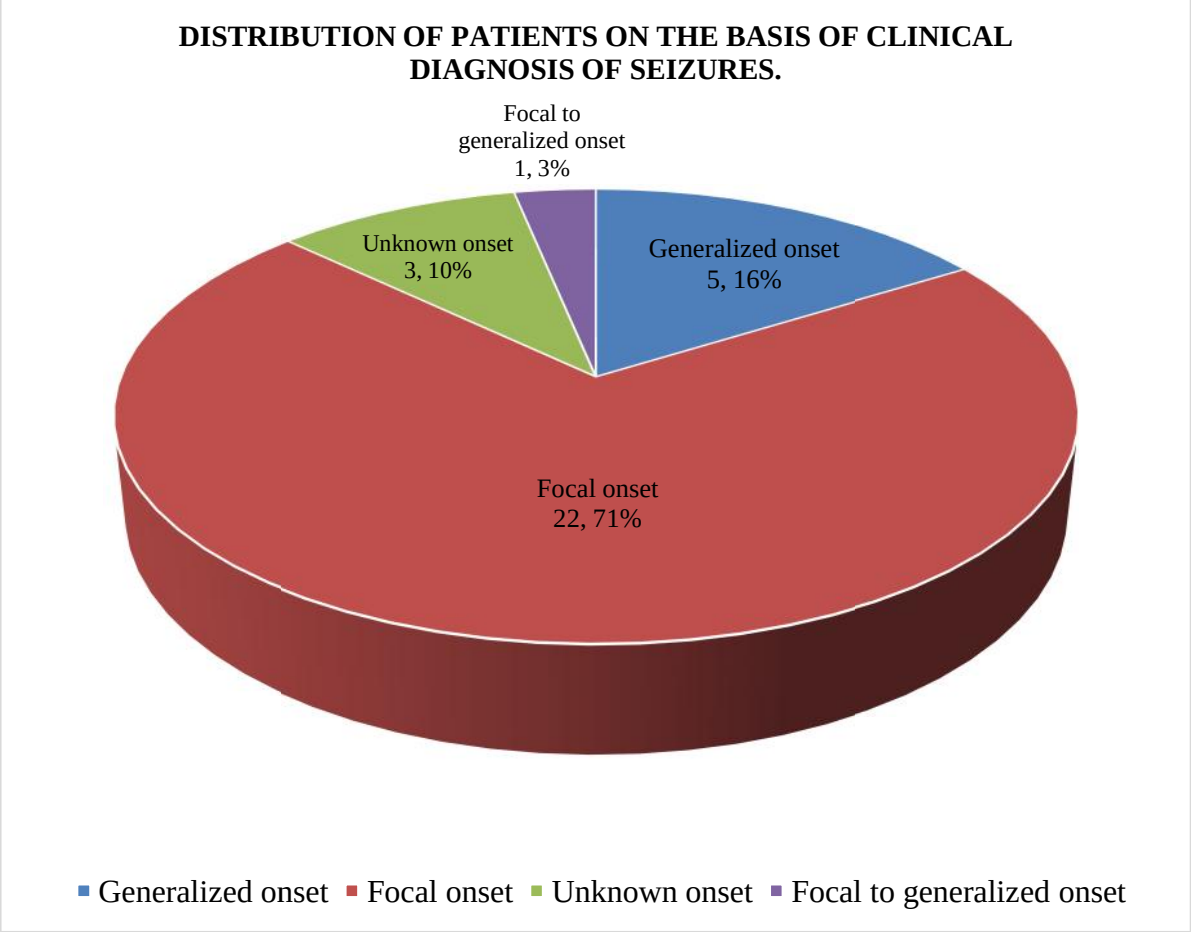


TABLE -3 DISTRIBUTION OF PATIENTS ON THE BASIS OF DURATION OF SEIZURES

Duration of Seizure (min)	No. of patients	Percentage
≤ 1	6	19.35
2	13	41.94
3	8	25.81
≥ 4	4	12.90
TOTAL	31	100.00

Most of the children presented with seizures of 2 minute duration.

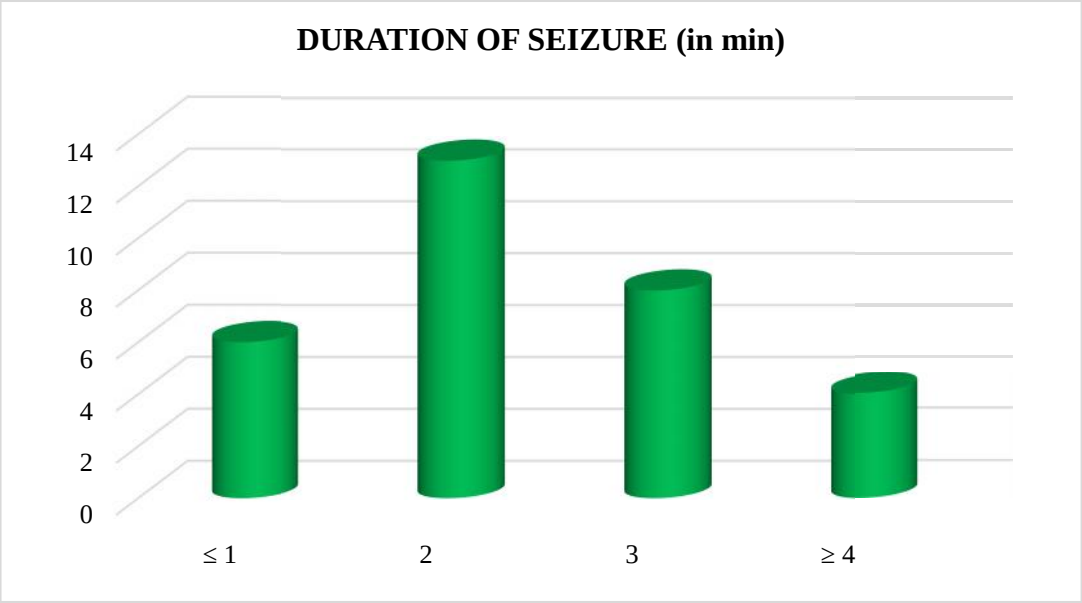


TABLE -4 DISTRIBUTION OF PATIENTS ON MR DIAGNOSIS

MR diagnosis	NUMBER	PERCENTAGE
Structural Malformation	4	12.90
Stroke	1	3.23
Infective	2	6.45
Hemorrhage	1	3.23
Encephalomalacia	2	6.45
Malformations, vascular	1	3.23
Atrophy	2	6.45
Mesial temporal sclerosis	1	3.23
Metabolic / Inborn errors	4	12.90
Periventricular leukomalacia	1	3.23
Normal	12	38.70
TOTAL	31	100.00

In 11 out of 31 children (35.48 %), the study was normal. In 4 children (12.90 %) structural malformations was noted.

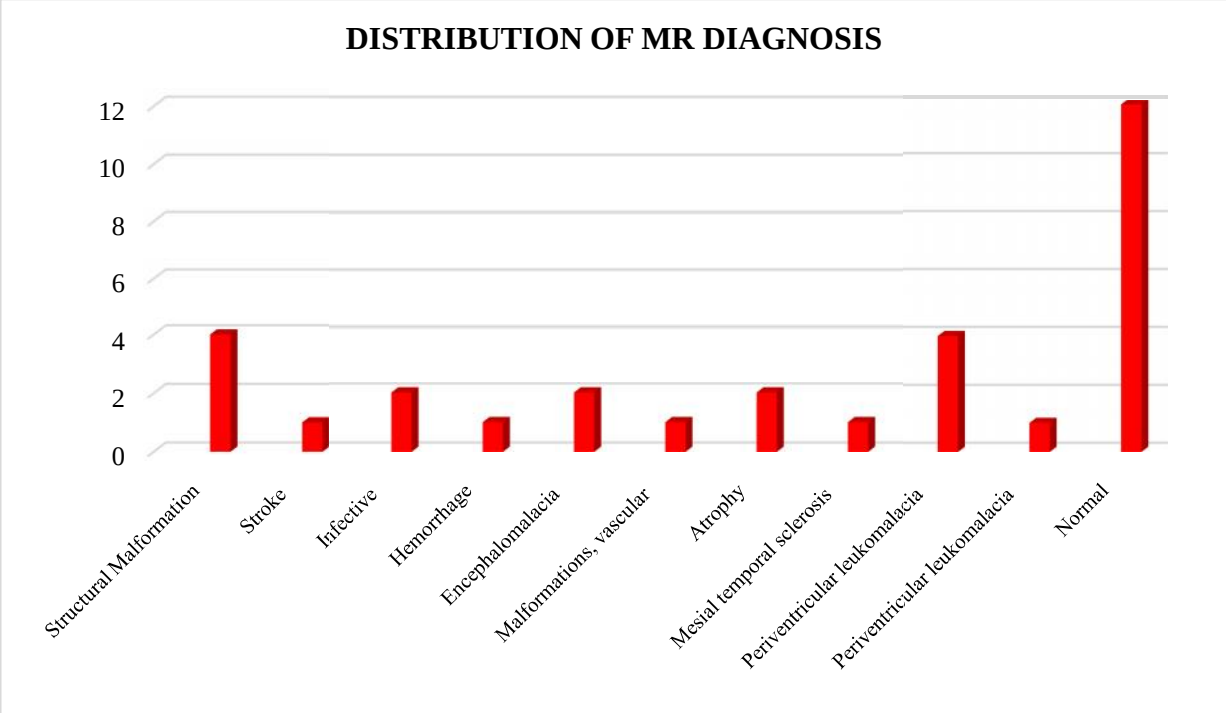


TABLE -5 PERCENTAGE OF ABNORMAL MR DIAGNOSIS

Total	Normal	Percentage	Abnormal	Percentage
31	12	38.71	19	61.29

In 31 children with first onset seizures, 19 children (61.29 %) showed magnetic resonance imaging abnormalities.

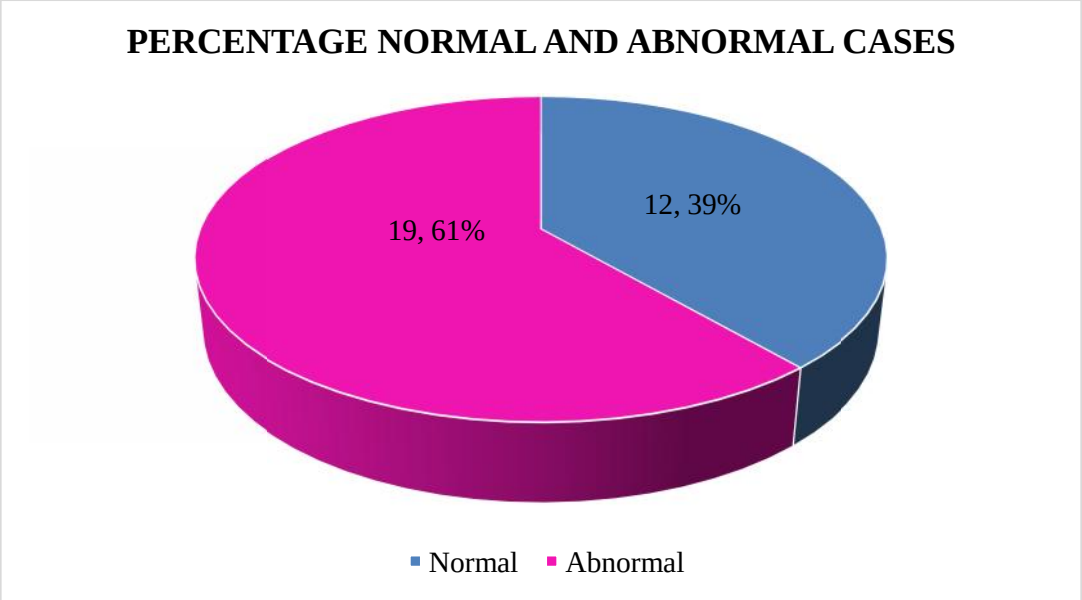


TABLE-6 : DISTRIBUTION OF ABNORMALITIES ON SEX WISE DISTRIBUTION

	NUMBER	PERCENTAGE
Male	11	57.90
Female	8	42.10
Total	19	100

11 males (57.90%) and 8 females(42.10%) were found to have abnormal findings out of 31 patients.

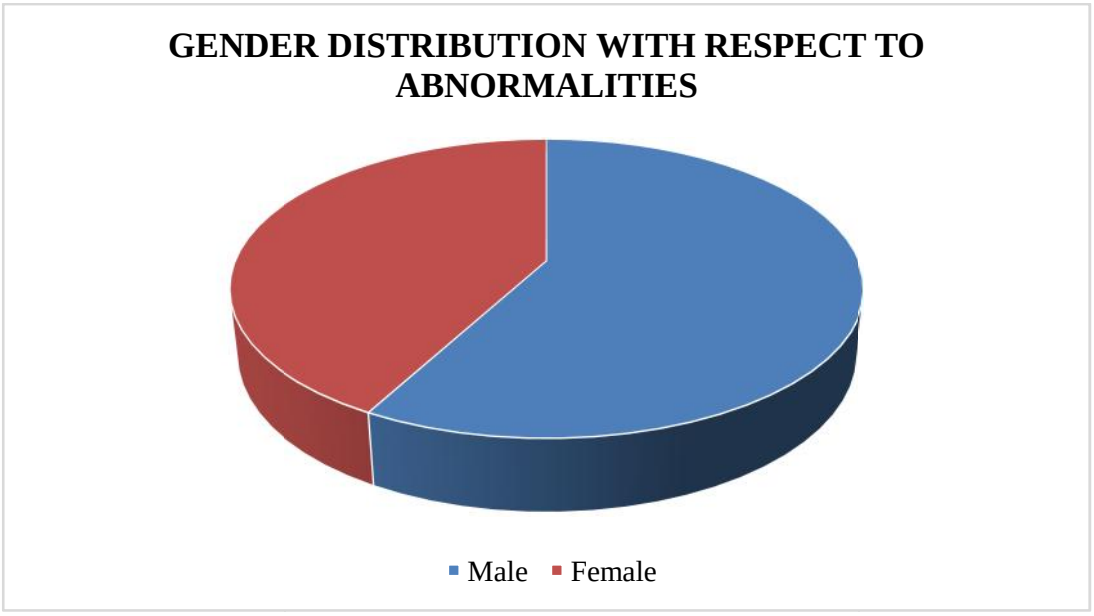


TABLE-7 DISTRIBUTION OF ABNORMALITIES IN VARIOUS AGE GROUPS

	AGE (MONTHS)				
MR diagnosis	**1 - 6**	**7 - 12**	**13 - 18**	**19 - 24**	**TOTAL**
Structural Malformation	2	0	0	2	4
Stroke	1	0	0	0	1
Infective	1	1	0	0	2
Hemorrhage	1	0	0	0	1
Encephalomalacia	1	1	0	0	2
Malformations, vascular	0	0	1	0	1
Atrophy	1	1	0	0	2
Mesial temporal sclerosis	0	1	0	0	1
Metabolic / inborn errors	3	0	1	0	4
Periventricular leukomalacia	0	1	0	0	1
Normal	3	5	2	2	12
TOTAL	13	10	4	4	31

Imaging abnormalities were noted maximum in the children between 0-6 months of age.

TABLE-8 : SPECTROSCOPY FINDINGS IN THE PATIENTS

No. of patients	Normal	Abnormal	total
Spectroscopy findings	22 (70.96%)	9(29.0%)	31

Out of 31 patients, 22 showed normal spectroscopy and 9 patients showed abnormal spectroscopy changes.

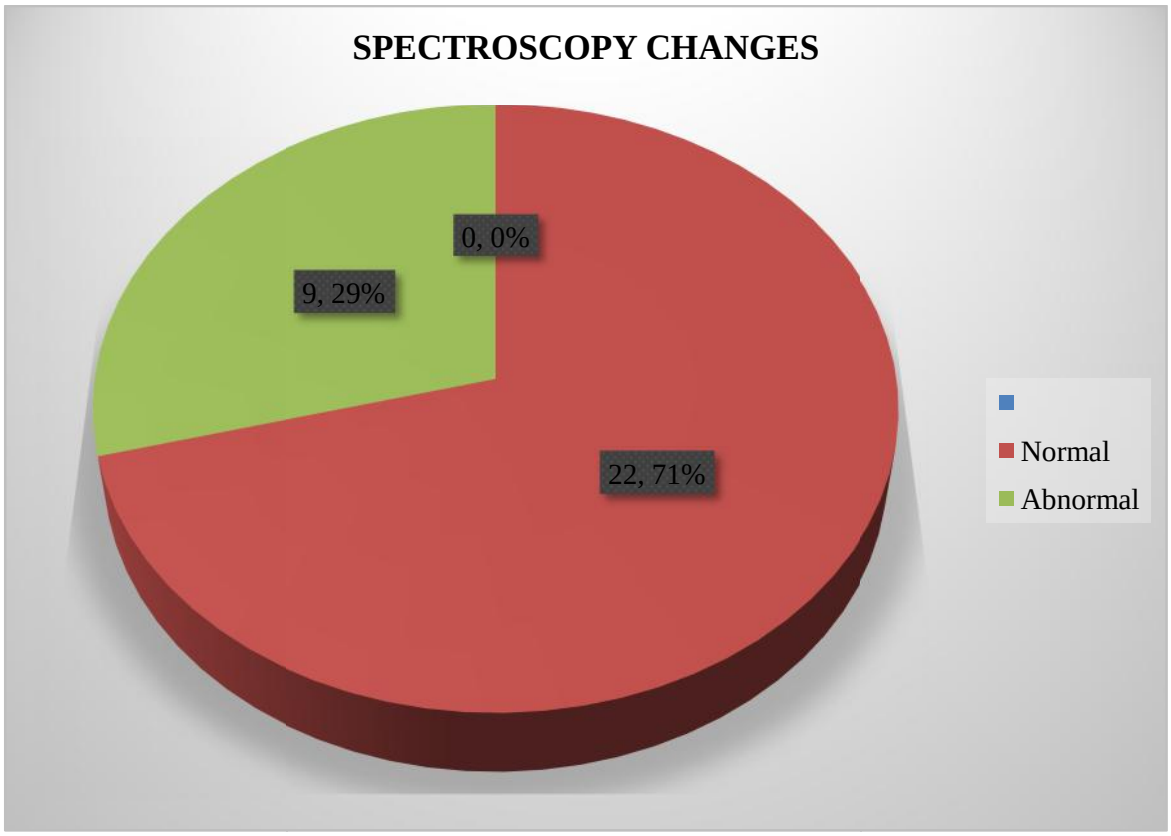
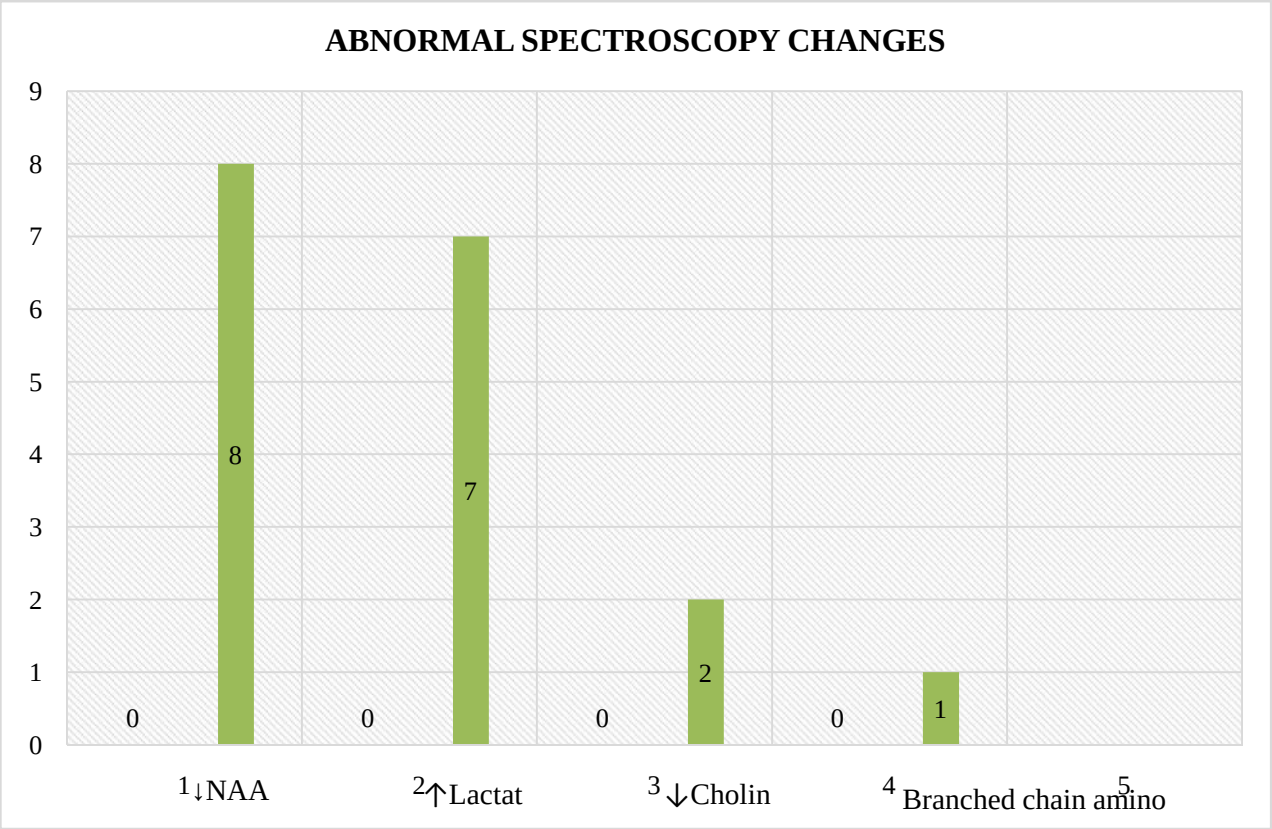


TABLE 9- ABNORMAL SPECTROSCOPY CHANGES

Findings	↓NAA	↑Lactate	↓Choline	Branched chain amino acids
No. of patients	8	7	2	1

Out of 9 patients who had abnormal spectroscopy changes,



DISCUSSION

Children presenting with first onset seizures can have various wide range of magnetic resonance imaging abnormalities depending upon the underlying causes. MRI can adequately identify the cause and etiology for the seizures and thus help in further management of the children[42].

In our study with 31 children with diagnosis of first onset seizures clinically were selected as per criteria put down by 'ILAE' 2017.

The clinical history of each child was verified and all underwent biochemical investigations. MRI scan was carried out with 1.5 T & 3.0 T PHILIPS MRI scanner.

Patients presented with seizures of different durations ranging from 30s to 5 min. Focal partial seizures were the most common type infants presented with.

The MR imaging revealed abnormal findings in 19 out of 31 patients which included structural malformations (cerebral dysgenesis) (12.90%), metabolic errors (12.90%), atrophy (9.68%), infective etiology (6.45%), encephalomalacic changes (6.45%), stroke (3.23%), hemorrhage (3.23%), vascular malformations(3.23%),

Structural Malformations (Cerebral dysgenesis):

4 infants with new onset seizures showed structural malformations. One infant revealed enlargement of the occipital horns of bilateral lateral ventricles which was suggestive of colpocephaly with complete agenesis of the corpus callosum.

One infant revealed well defined T2 hyperintense & T1 hypointense cystic area in the right anterior temporal region suggestive of arachnoid cyst. The cyst was seen to cause compression on the adjacent temporal brain parenchyma.

One infant revealed dysgenesis of the corpus callosum with severe thinning of the corpus callosum in its entire length. There were features of hypoxic injury such as encephalomalacic changes.

One infant with global developmental delay showed broad gyri in the fronto-temporo-parietal regions with smooth brain parenchyma surface which distinguished it as Type-I lissencephaly. Bilateral lateral ventricles appeared prominent for age.

Metabolic errors:

4 infants with new onset seizures showed imaging abnormalities which were due to inborn metabolic errors.

Two infants showed T2 and FLAIR hyperintensities in the bilateral parieto-occipital regions and splenium of corpus callosum which were diagnosed as hypoglycemic encephalopathy.

One infant showed T2 hyperintense and T1 hypointense areas with diffusion restriction involving sub cortical white matter of posterior parieto-occipital region, posterior limb of internal capsule, bilateral thalami, bilateral cerebral peduncles, middle cerebral peduncle, dorsal brainstem, cerebellar white matter (sparing the dentate nuclei). These features were suggestive of maple syrup urine disease.

Maple syrup urine disease is a metabolic disorder which affects the branched chain amino acids. MR spectroscopy showed amino acid peak at 0.9-1.0 ppm.

One infant revealed T2 and FLAIR hyperintensities with diffusion restriction in the right temporo-parietal regions, bilateral occipital regions and bilateral medial temporal lobes which suggested mitochondrial encephalopathy.

Infective etiology: One infant with first onset seizure showed well defined central T2 hyperintense & FLAIR hypointense lesions with peripheral FLAIR hyperintense rings in the bilateral frontal and left parietal regions with peripheral restriction on DWI sequence. There was mild proptosis of the right eye ball with T2 and FLAIR subretinal exudates. Areas of diffusion restriction were also noted along the occipital horn of right lateral ventricle. Infant was diagnosed as cerebral abscesses with ependymitis. On MRS, Lipid-lactate peak was noted at the 1.3 ppm.

One infant had multiple symmetrical T2 & FLAIR hyperintense and T1 hypointense areas which shows diffusion restriction on DWI sequence in the bilateral thalami, basal ganglia, bilateral fronto-temporo-parietal & deep periventricular white matter, midbrain and tegmentum of pons. Hemorrhagic areas were noted in the head of bilateral caudate nucleus, left lentiform nucleus, bilateral thalami. The infant was diagnosed as acute necrotizing encephalitis.

D.T. Hsieh. et al[29], studied 317 infants presenting with new onset seizures and found the 29 infants (09.14%) had cerebral dysgenesis out of 208 infants with imaging abnormalities.

Shlomo Shinnar. Et al[43], studied 407 children with first unprovoked afebrile seizure and found Cerebral dysgenesis including agenesis of corpus callosum, heterotropias and hamartoma in 5% of the patients.

Vieira SC et al[44], studied 500 cases with new onset seizures and found 4 cases to have cerebral dysgenesis.

Various studies have shown cerebral dysgenesis as the most common cause for new onset seizure with imaging abnormalities. However, few studies conducted in developing countries by Saini Narendra et al.[45] found infectious cases to be more common cause of new onset seizures.

Two infants showed brain atrophy in which one infant showed diffuse cerebral atrophy and the other infant showed cerebellar atrophy.

One infant showed subacute infarct in the cortical and subcortical frontal region, parieto-occipital watershed territory. One infant showed subdural hemorrhage in the bilateral fronto-temporo-parietal regions with bleeding diathesis disorder. One infant showed multiple T2 flow voids with perilesional edema in the right fronto-temporal regions which suggested arterio-venous malformation. Two infants showed cerebral cystic encephalomalacic changes with thinning of the cortex.

One infant with new onset seizure showed changes of mesial temporal sclerosis and one infant showed changes of periventricular leukomalacia. In the study conducted by D.T. Hsieh. et al[29], 6 infants showed changes of periventricular leukomalacia.

CONCLUSION

Precise diagnosis of the cause of seizure is vital for finding an effective treatment. MRI has been shown to be highly sensitive and specific in recognizing the underlying pathology in seizures. With its high spatial resolution, excellent inherent soft tissue contrast, multipanar imaging capability and lack of ionizing radiation, MR imaging has emerged as a resourceful tool in the evaluation of patients with seizures.

Routine use of magnetic resonance imaging after first onset seizures helps to identify the underlying pathophysiological causes and its severity and thus helping in further medical and surgical management.

As per our study, use of MRI with spectroscopy resulted in early detection of the structural malformations, inborn metabolic errors, infectious causes and also other various causes resulting in prompt definitive treatment.

These results suggest that Use of MRI with spectroscopy can be used as a routine screening tool for assessment of the new onset seizures in the neonatal life.

Studies with a larger sample size with immediate and long term follow-up is required to include routine MRI screening as a modality after new onset seizure.

Future studies could compare the use of MRI and EEG for better diagnosis of the pathophysiology thus resulting in prompt accurate treatment protocol.

SUMMARY

In our study 31 infants who were clinically diagnosed with new onset seizure were undergone MRI examination of the brain with spectroscopy.

The imaging features were normal in 12 patients (38.70%). 19 patients had imaging abnormalities. Common abnormalities were structural abnormalities (12.90%) and inborn metabolic errors (12.90%) followed by infectious causes (6.45%), cystic encephalomalacia (6.45%) and atrophy (6.45%). Rest of the abnormalities included vascular malformations, stroke, hemorrhage and mesial temporal sclerosis.

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ANNEXURE I-CONSENT FORM

INFORMED CONSENT

TITLE OF THE STUDY: "YIELD OF MAGNETIC RESONANCE IMAGING WITH SPECTROSCOPY IN CHILDREN WITH NEW ONSET AFEBRILE SEIZURE BETWEEN ONE MONTH TO TWENTY-FOUR MONTHS OF AGE"

PRINCIPAL INVESTIGATOR:

INTRODUCTION AND PURPOSE:

Seizures are symptoms of abnormal brain function and due to a diverse etiology. Magnetic Resonance Imaging (MRI) is the current imaging tool of choice in the investigation of patients with seizures. The advent of high resolution MRI with a dedicated seizure protocol has significantly increased the chances of identifying a cause resulting in a positive clinical impact on the management of these patients.

PROCEDURE:

I request you to kindly participate in the study titled study "**Yield of magnetic resonance imaging with spectroscopy in children with new onset afebrile seizure between one month to twenty four months of age**" at Dr. Prabhakar Kore charitable hospital and Medical Research Centre, Belgaum" is being conducted by Dr. _____ post graduate in Radio diagnosis at J. N. Medical College Belgaum, Karnataka, under the guidance of Dr. _____, Professor, Dept. of Radio diagnosis, J. N. Medical College, Belgaum.

We request you to participate in this study as you are eligible to be included. During the study you will be asked questions regarding your present and past medical history and you will be required to answer to the best of your knowledge. U will also be clinically examined as per the protocol drawn.

If you agree to participate in the study, please furnish the details pertaining to the study.

BENEFITS:

- Noninvasive modality

COMPLICATIONS:

- No risk to the patient has been documented from MR imaging of the brain conducted earlier.

ALTERNATIVES:

If patient is not willing to take part in the study, his / her treatment or any other further investigations the patient wants to undergo, in future, in KLE will not be affected by his / her decision.

VOLUNTARY PARTICIPATION/WITHDRAWAL:

Taking part in this study is voluntary. I may choose not to take part in this study, or if I decide to take part I can later change my mind and withdraw from the study. My decision will not change the present or future health care or other services that I receive. The study doctor or the sponsor may stop my participation in this study. I will tell if any important new findings that may change my

willingness to continue to take part. If I choose not to take part in the study I will receive the standard treatment for patients with my condition.

COSTS:

NIL (The study is to be conducted on the participants who are advised MRI as a investigation for low backache by the referring consultant and the participants will bear the charges for it.)

Payment for Participation: No incentive will be paid to you for participating in this study.

COMPENSATION:

In the event that I become injured as a result of taking part in this study, treatment whatever available at KLE charitable hospital, Belagavi, will be offered to me. No reimbursement, compensation or free medical care is given.

CONFIDENTIALITY:

All information collected about me during the course of the study will be kept confidential to the extent permitted by the law. The code numbers will identify me in this research record. Information from this study may be published but my identity will be confidential in any publication.

QUESTION:

If any enquiries in the future or in case of research related injury illness, you may contact following person.

Dr. Roopa M Bellad Professor and Unit Head Of Pediatrics Chairman, J.N. Medical College Institutional Ethical Committee for Human Subjects Research Ph. No: 0831-2473777, Ext. 1529

CONSENT TO PARTICIPATE IN RESEARCH STUDY:

1. I understand that I am participating in the study, which includes Magnetic Resonance Imaging of brain.

2. I confirm that I have read and understood the information in the patient information sheet. Procedure is explained to me in detail along with information about the advantages and disadvantages of taking part in the study. I have been given the opportunity to discuss all aspects of the trial, to ask questions and hereby consent to participation in the trial outlined above.

3. I understand that the decision to take part in this study is completely voluntary and I am aware that I can choose to withdraw from the study at any point of time.

4. I consent to the photographing or recording of the procedure to be performed including appropriate portions of my body, for medical, scientific

or educational purposes provided my identity is not revealed in the pictures or by the descriptive texts accompanying them.

5. I understand that there is no significant risk involved in the test that would be done in this study.

6. No guarantee or assurance has given by anyone as to the results that may be obtained.

7. My signature on this form signifies that I have willingly decided to participate after understanding the above information.

Participant's Name/ legally authorized representative _____

Signature _____

Name and signature of witness _____

Name and signature of interviewer _____

Date:

Place:

1. My signature on this form signifies that I have willingly decided to participate after understanding the above information.

Participant's / legally authorized representatives name_____

Signature _____

Name and signature of witness _____

Investigators name and Signature: …….

Date:

Place: Belagavi

ANNEXURE II- ETHICAL CLEARANCE LETTER

K.L.E.UNIVERSITY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
(Accredited 'A' Grade by NAAC)

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Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 07 **Date: 22/11/2017**

To,

PG student in Radiodiagnosis,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"YIELD OF MAGNETIC RESONANCE IMAGING WITH SPECTROSCOPY IN CHILDREN WITH NEW ONSET AFEBRILE SEIZURE BETWEEN ONE MONTH TO TWENTYFOUR MONTHS OF AGE",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE III-PROFORMA

PROFORMA FOR DATA COLLECTION

Name_____

Age_____ **OP/IP NO _____**

Mobile_____

Address _____

_____

MRI number: _____

Chief complaints:

History of presenting illness

a) Seizures

a) Duration:

b) Type

b) Vomiting

c) Altered sensorium

d) Post ictal state

e) History of trauma

f) History of fever

g) Others (if any)

Past history

Family history

PROVISIONAL / CLINICALDIAGNOSIS:

MRISCAN:

Date Sl.No.

a) Spin echo-images T1WI T2 WI

B) FLAIR

c) DWI with ADC

d) MRS

e) Gradient Echo-sequence

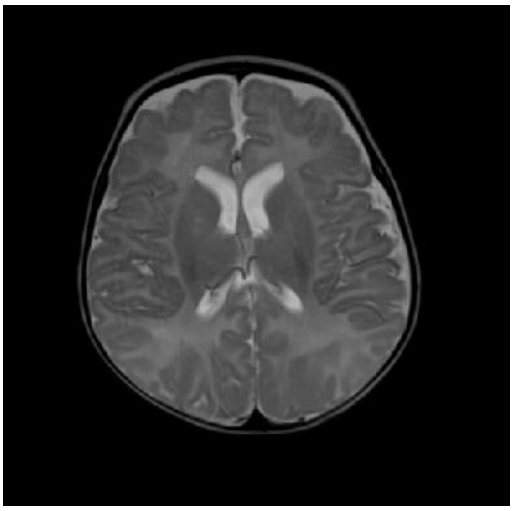
f) T1 with contrast

MRI –DIAGNOSIS:

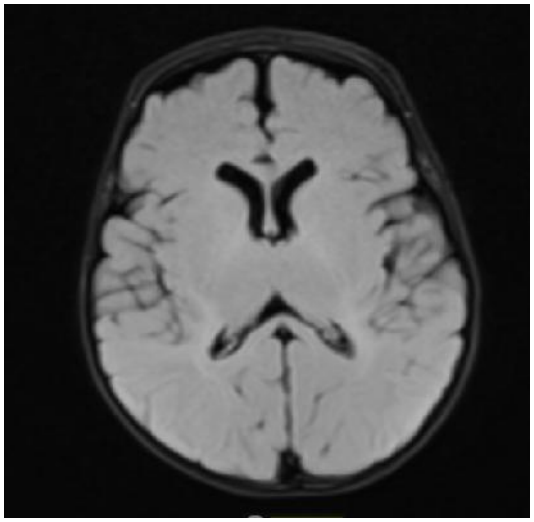
TREATMENT:

FOLLOWUP:

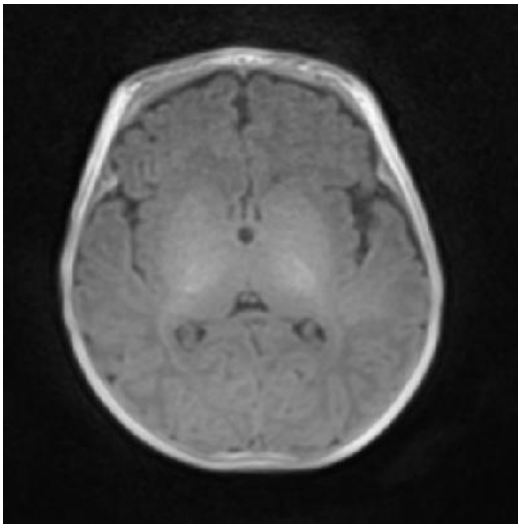
ANNEXURE IV: FIGURES



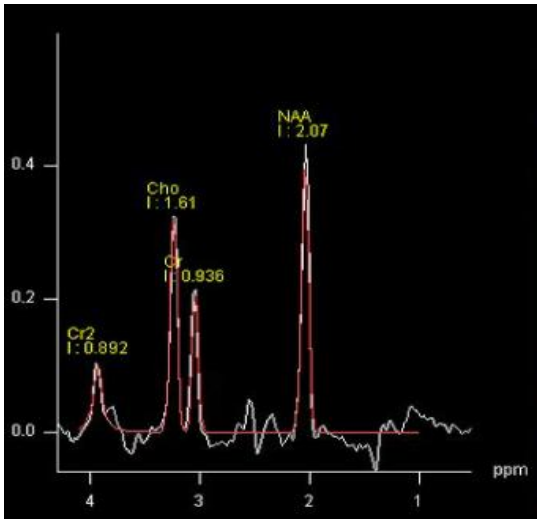
T2- Weighted Sequence



FLAIR Sequence

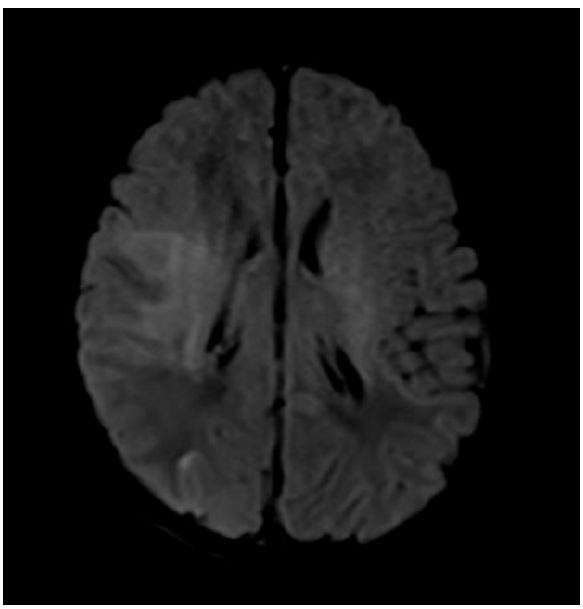


MP-RAGE Sequence

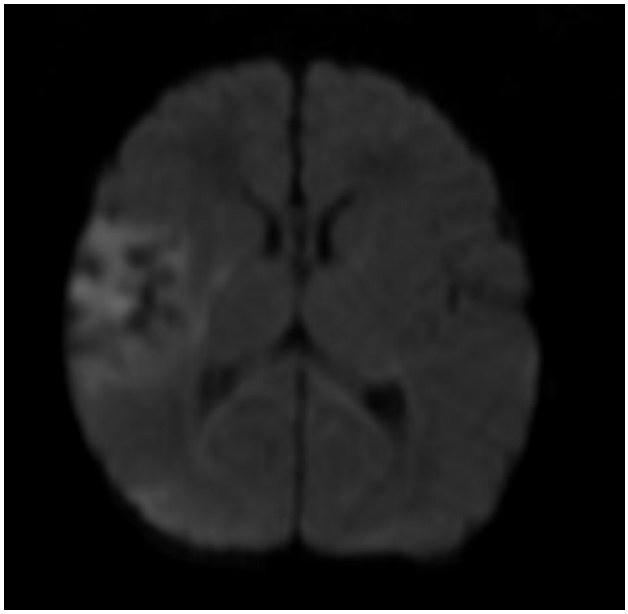


Normal Spectroscopy

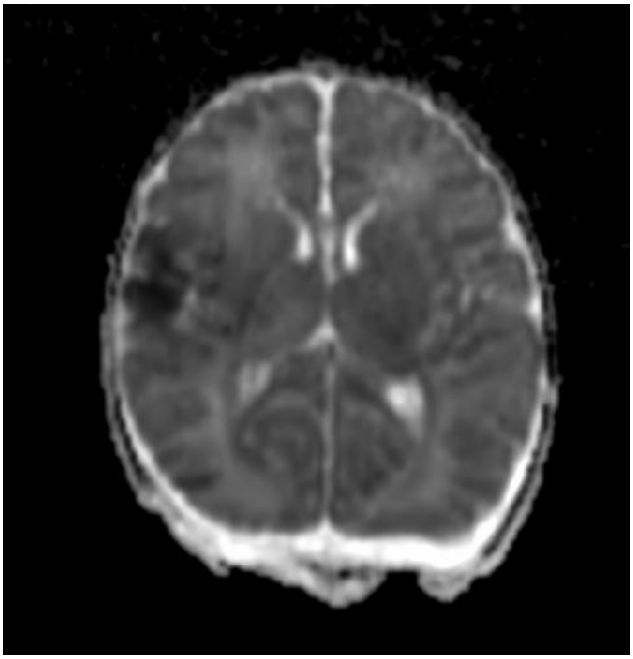
Fig 4. MRI OF NORMAL BRAIN.



FLAIR

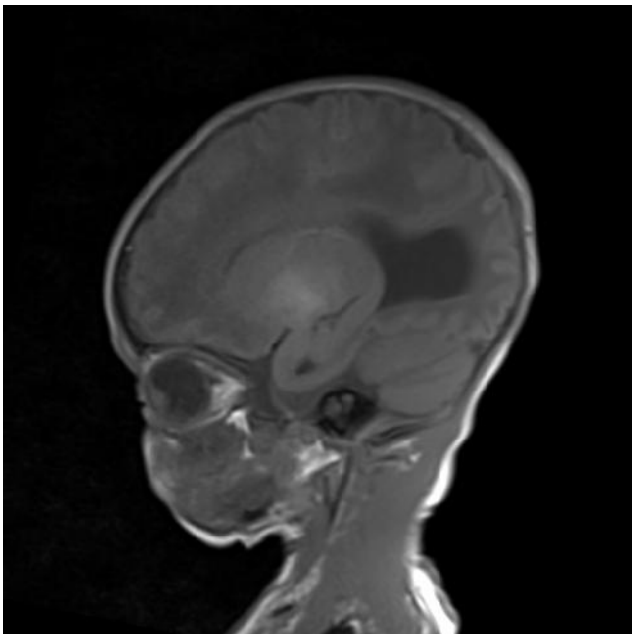


DWI

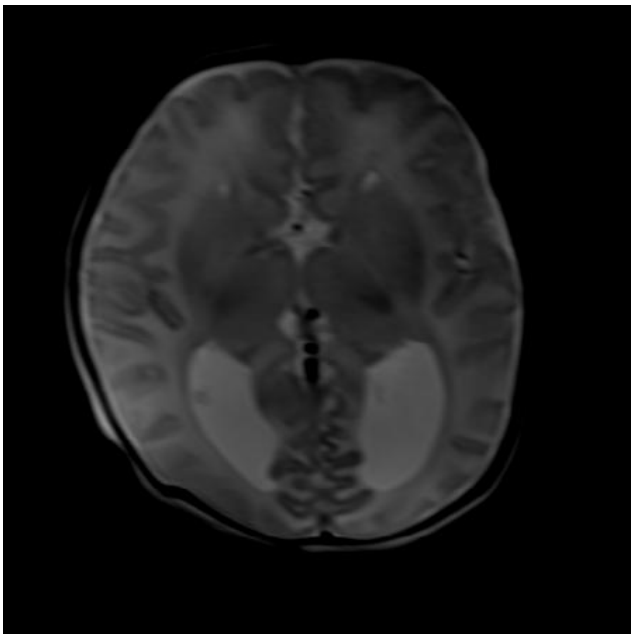


ADC

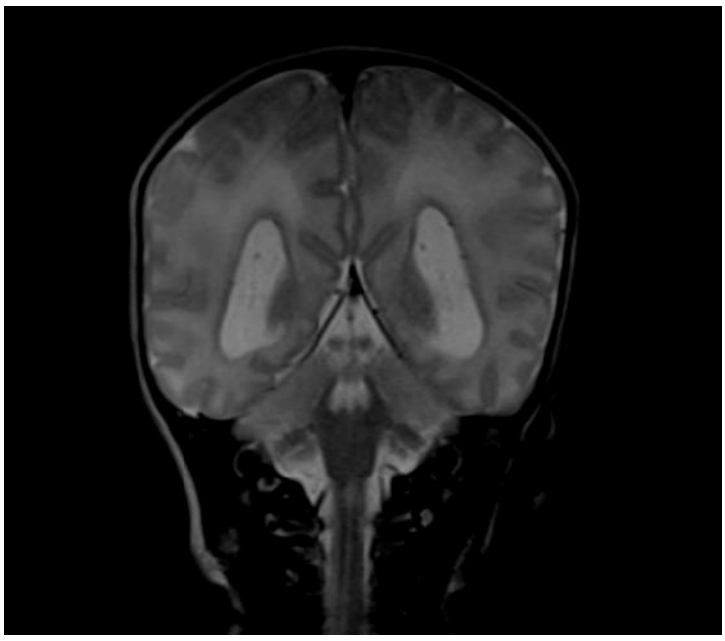
Figure 5- SUBACUTE INFARCT IN THE CORTICAL AND SUBCORTICAL FRONTAL REGION, PARIETO-OCCIPITAL WATERSHED TERRITORY



T1-SAGITTAL

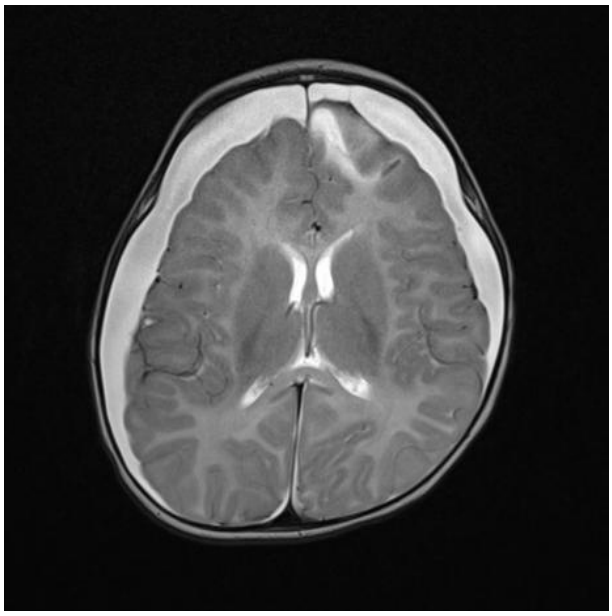


T2- AXIAL

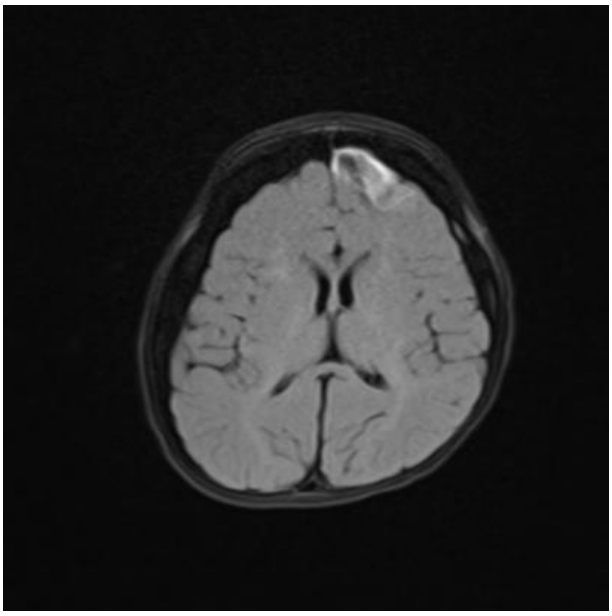


T2-CORONAL

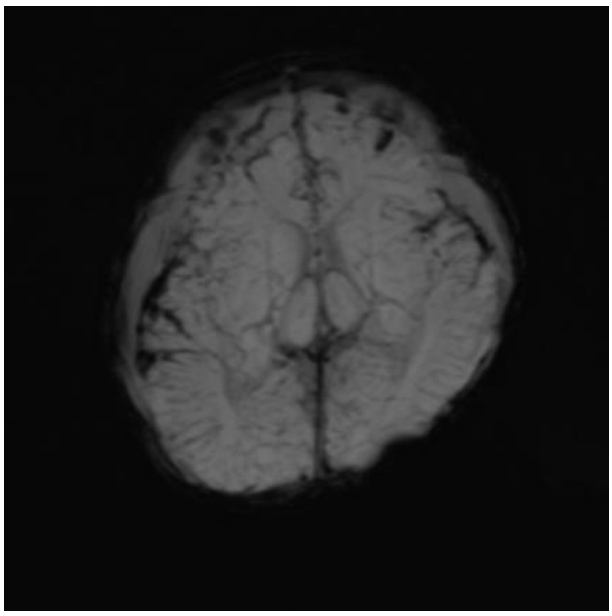
Fig 6: CORPUS CALLOSUM AGENESIS WITH COLPOCEPHALY



T2-AXIAL

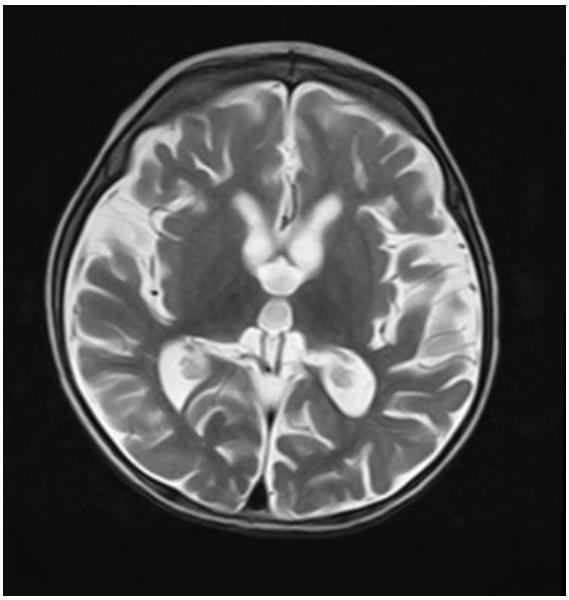


FLAIR-AXIAL

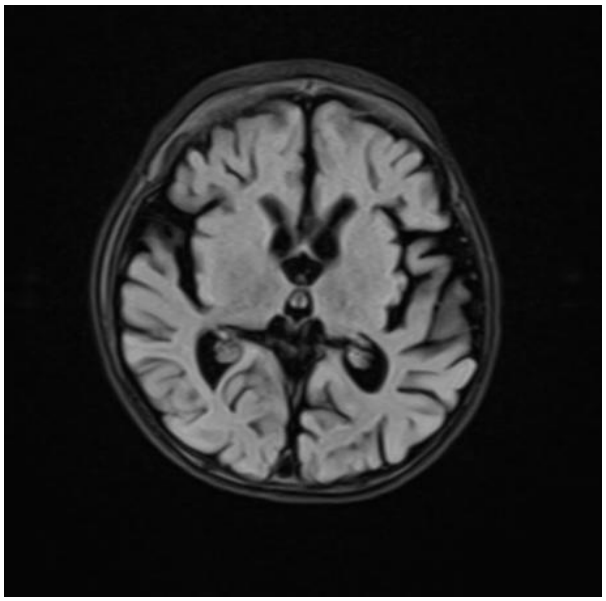


SWI

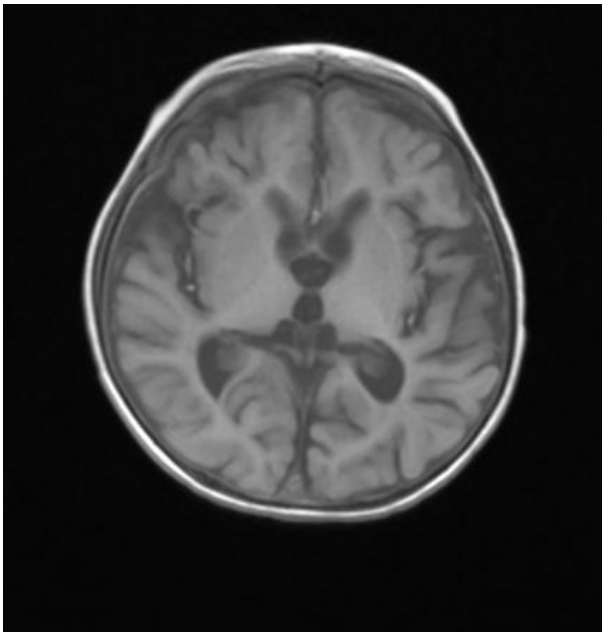
FIG 7: SUBDURAL HEMORRHAGE IN THE BILATERAL FRONTO-TEMPORO-PARIETAL REGIONS-BLEEDING DIATHESIS DISORDER



T2-AXIAL

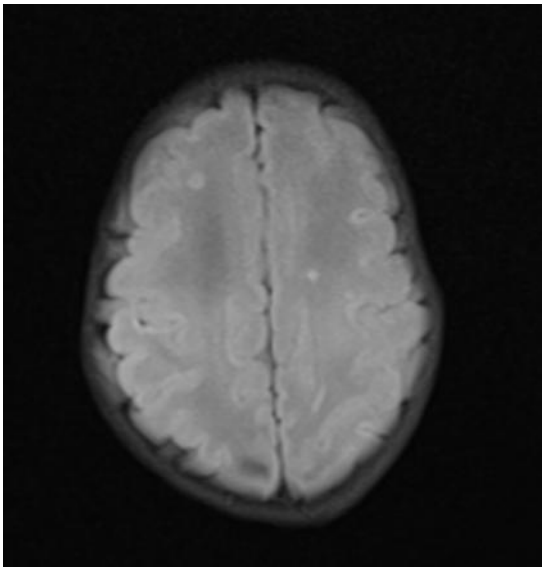


FLAIR-AXIAL

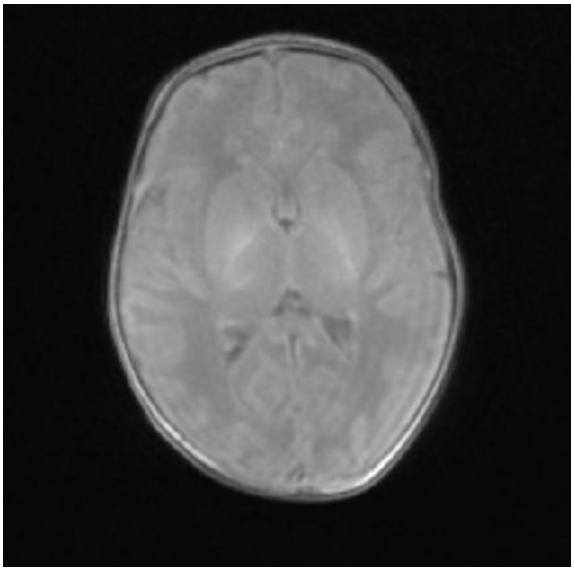


T1-AXIAL

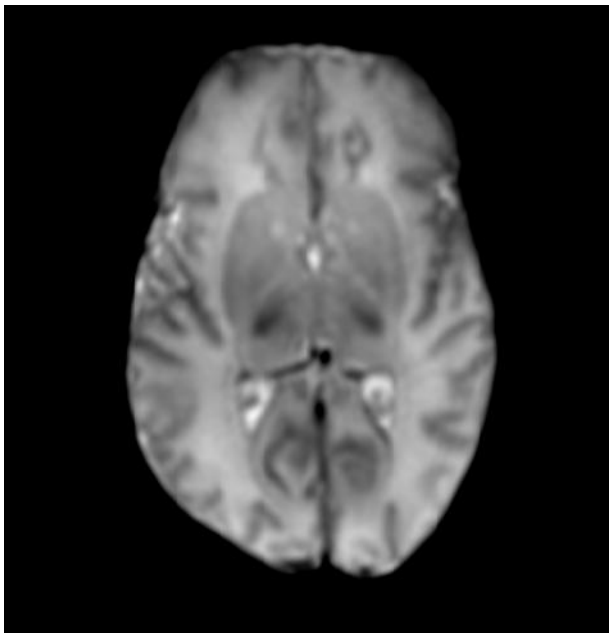
FIG 8: DIFFUSE CEREBRAL ATROPHY



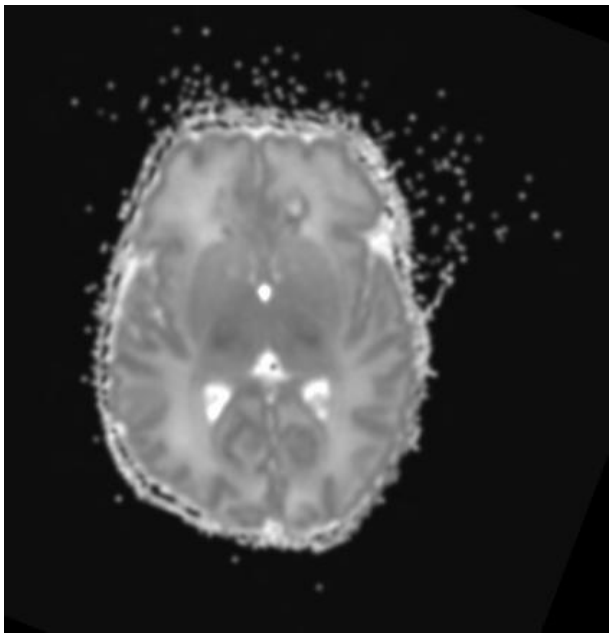
T1-AXIAL



T1-AXIAL



DWI



ADC

Fig 9: CEREBRAL ABSCESSES WITH EPENDYMITIS

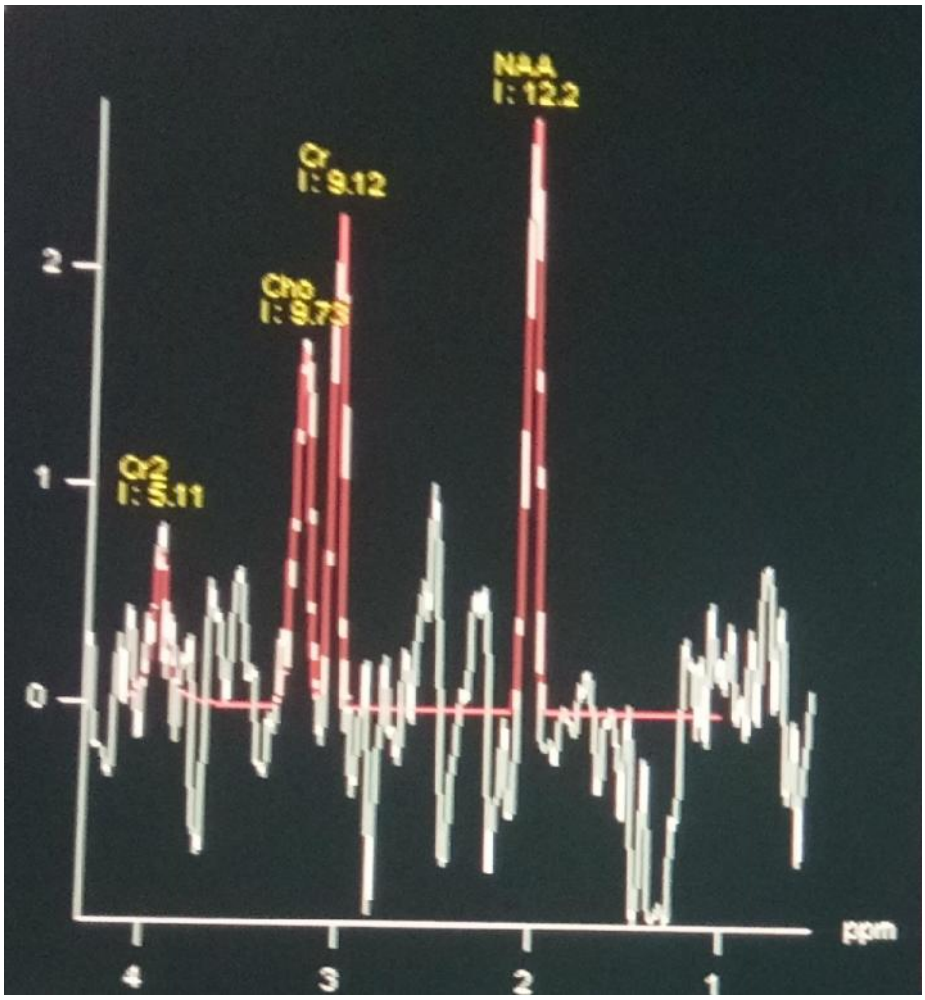
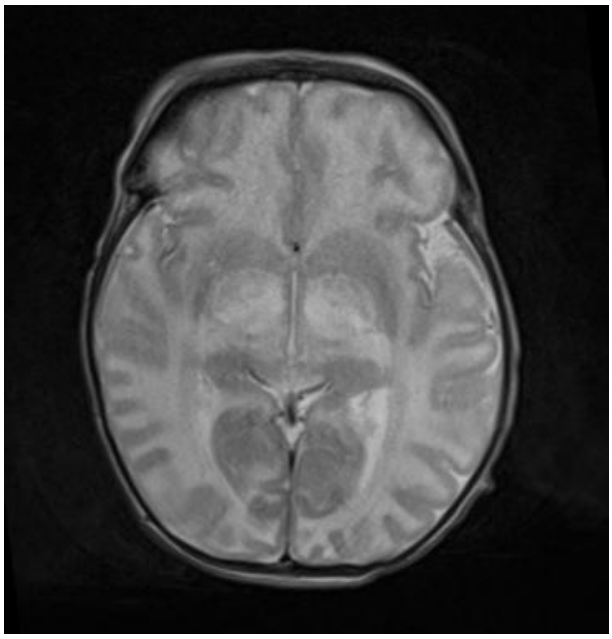
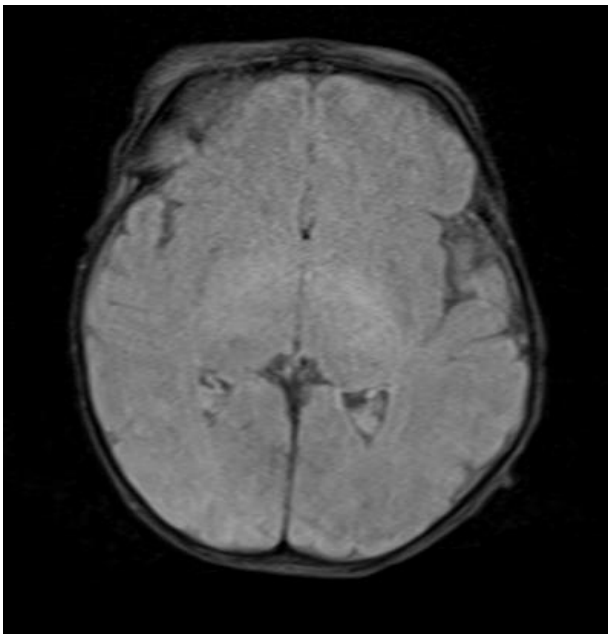


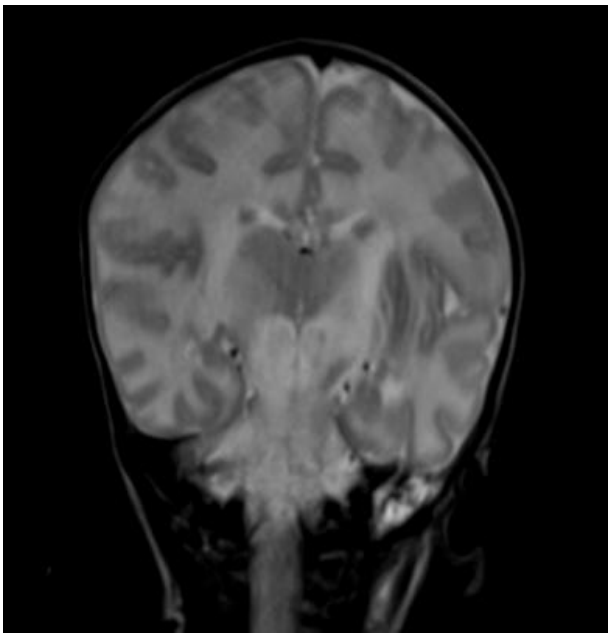
Fig 10: MR SPECTROSCOPY OF CEREBRAL ABSCESSES WITH EPENDYMITIS



T2-AXIAL

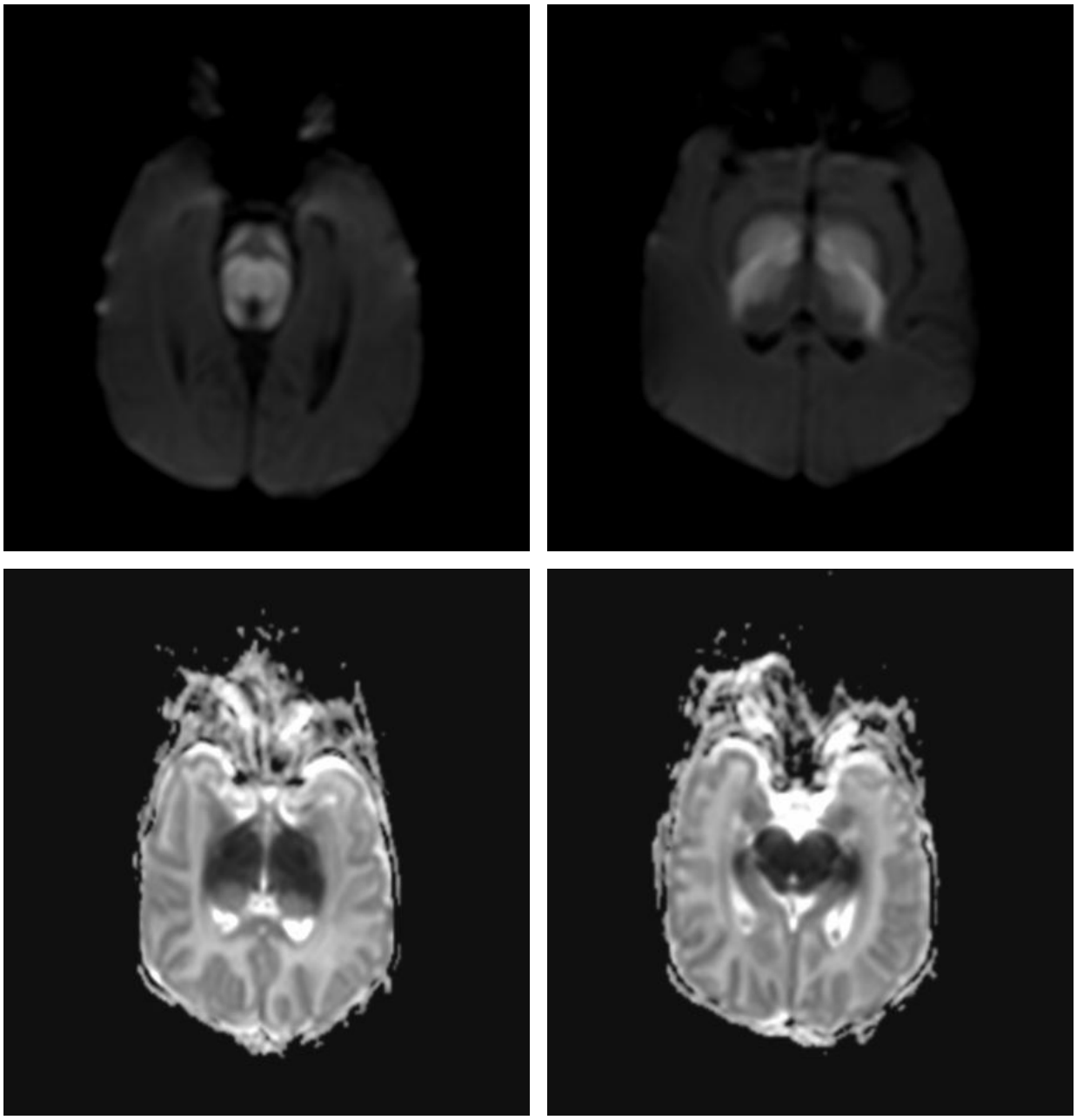


T1-AXIAL



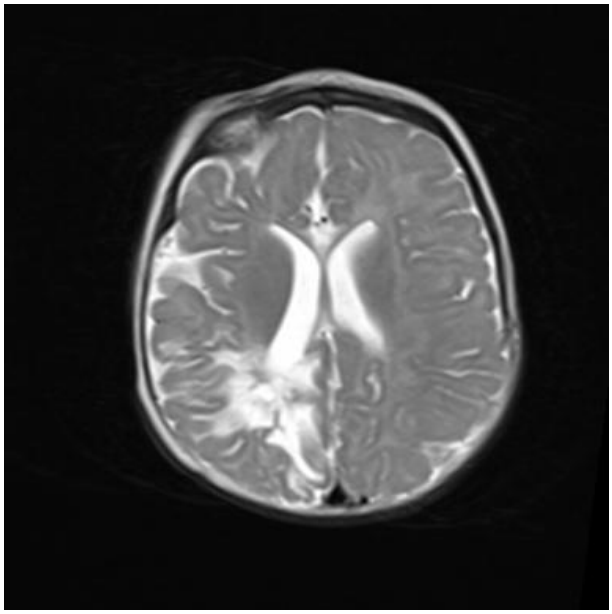
T2-CORONAL

Fig 11: MR IMAGES OF MAPLE SYRUP URINE DISEASE

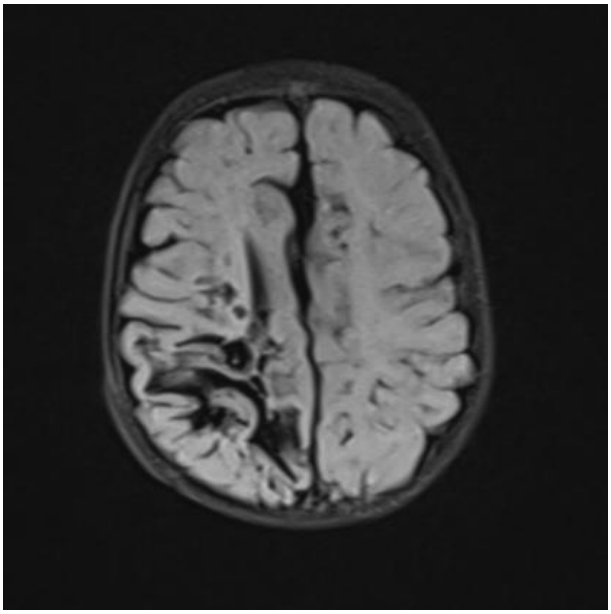


DWI AND ADC

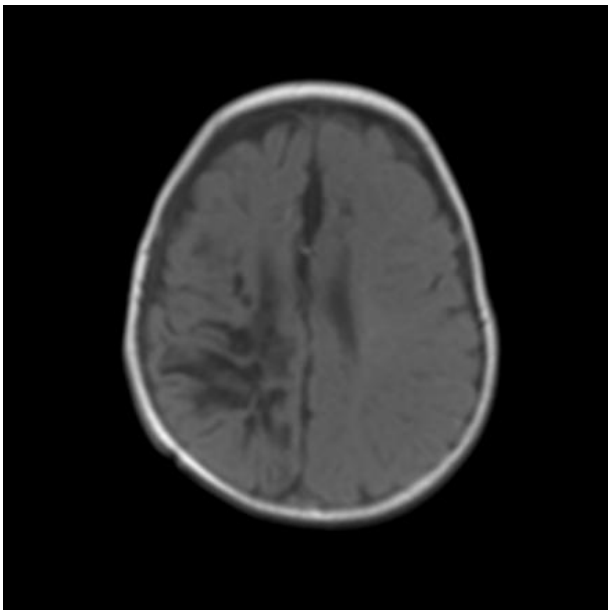
Fig 12: DIFFUSION WEIGHTED MR IMAGES OF MAPLE SYRUP URINE DISEASE



T2-AXIAL

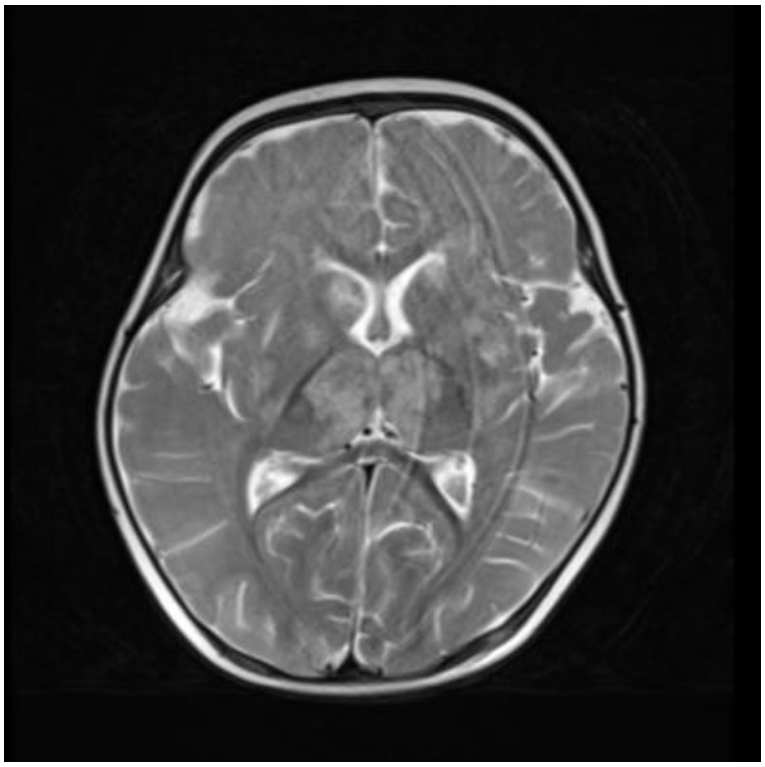


FLAIR-AXIAL

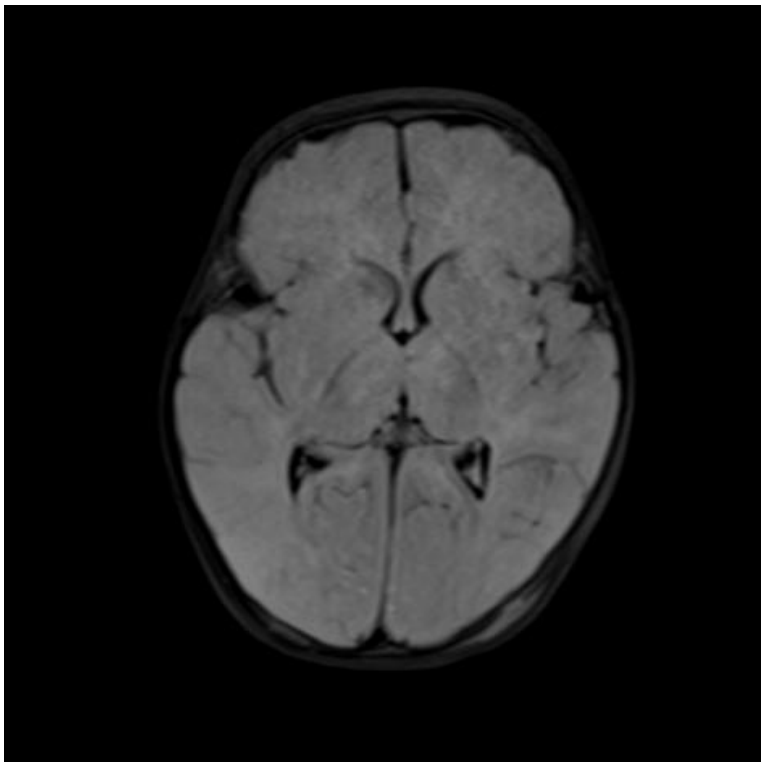


T1-AXIAL

Fig 13: CYSTIC ENCEPHALOMALACIA IN THE RIGHT FRONTO-PARIETAL REGION



T2-AXIAL



FLAIR-AXIAL

Fig 14: MRI IMAGING OF ACUTE NECROTIZING ENCEPHALITIS

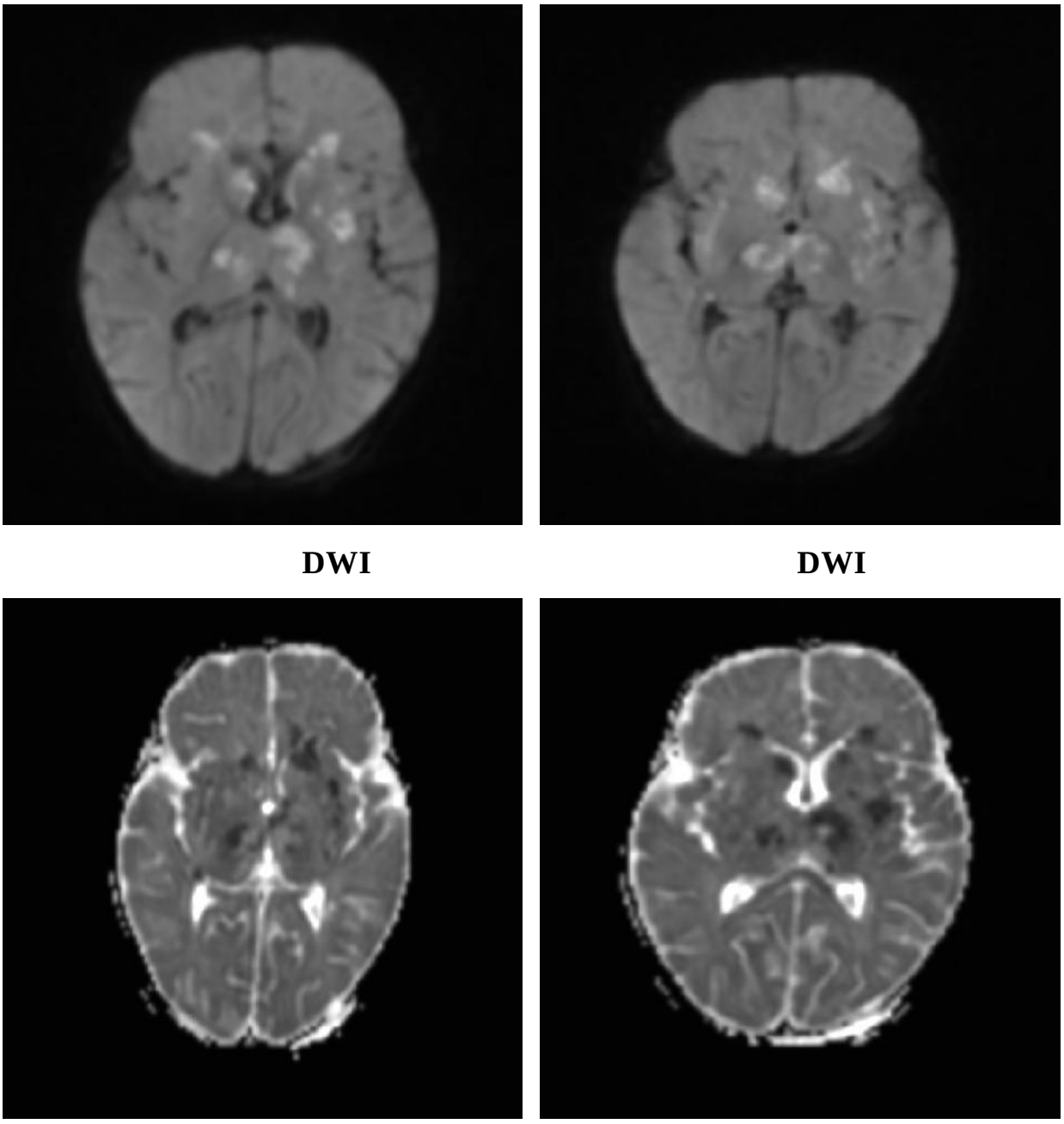
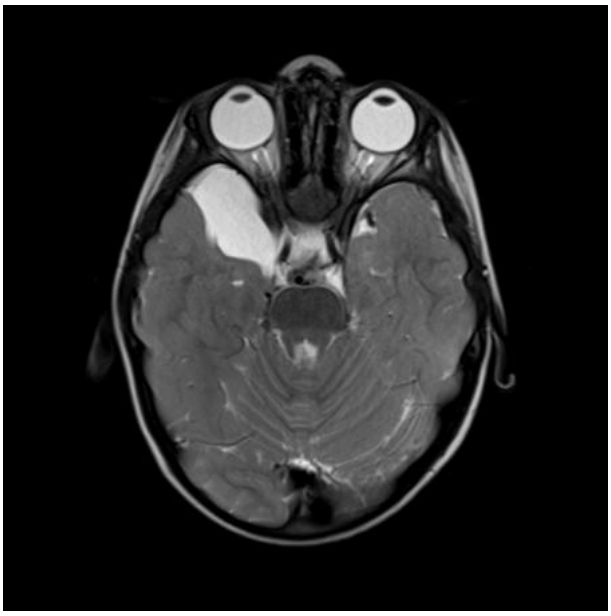
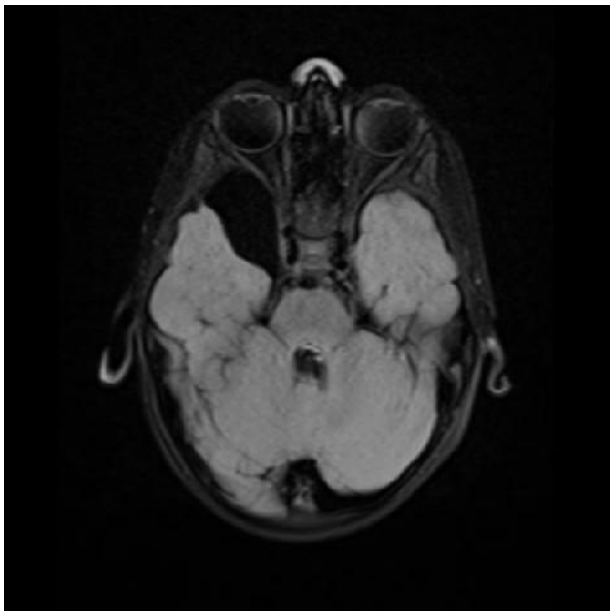


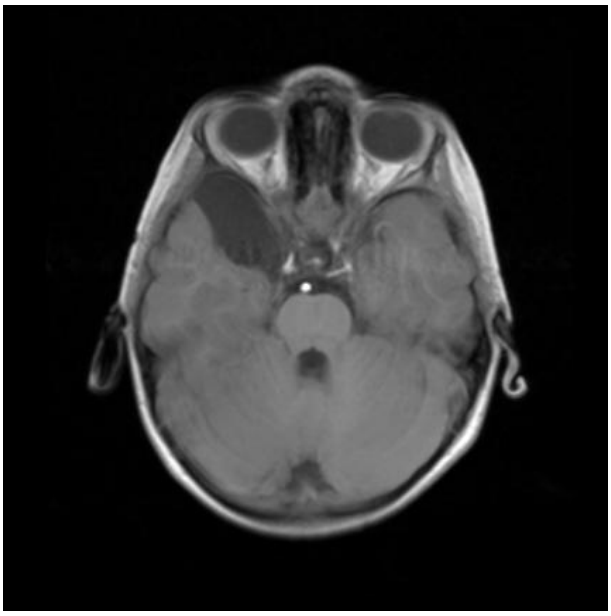
Fig 15: DIFFUSION WEIGHTED IMAGING OF ACUTE NECROTIZING ENCEPHALITIS



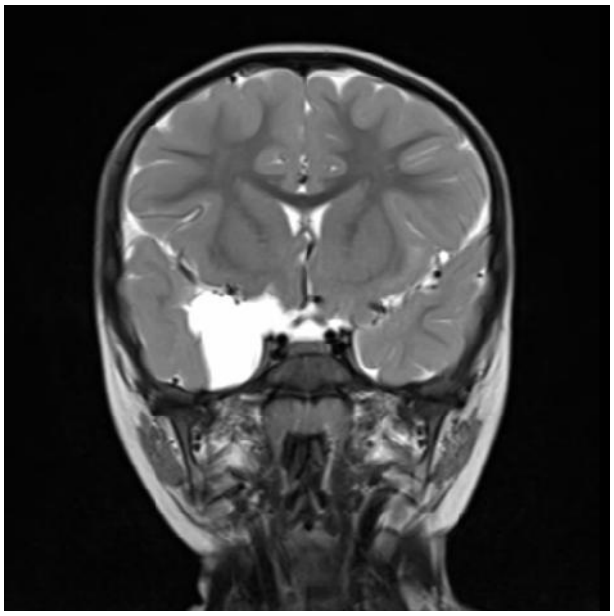
T2-AXIAL



FLAIR-AXIAL

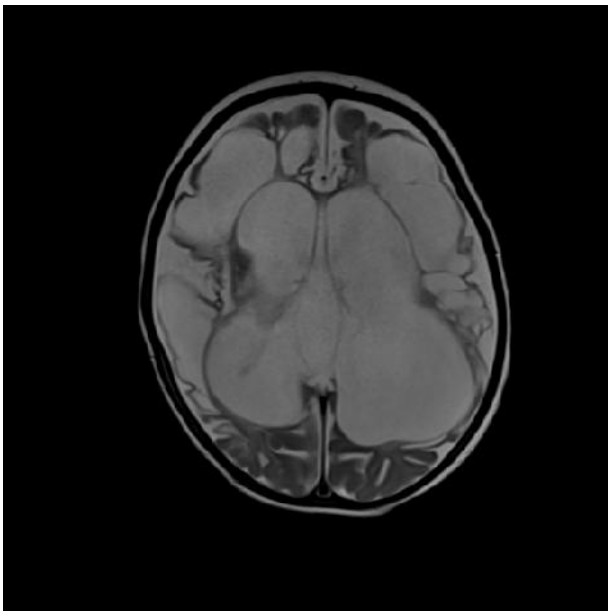


T1-AXIAL

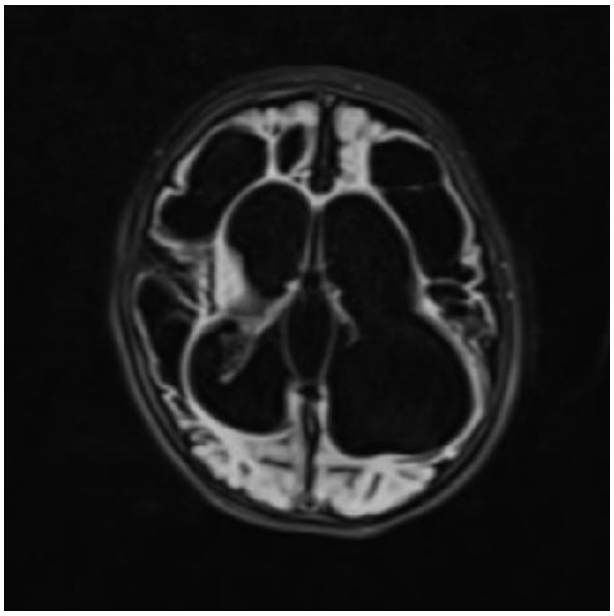


T2-CORONAL

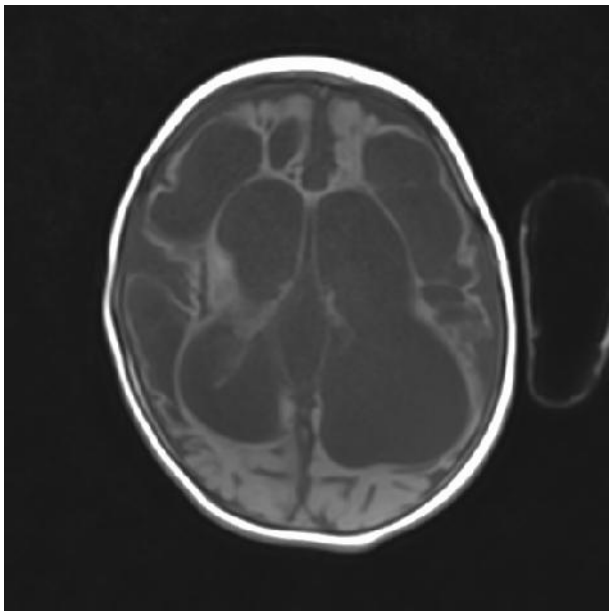
Fig 16: MRI IMAGES OF RIGHT ANTERIOR TEMPORAL ARACHNOID CYST



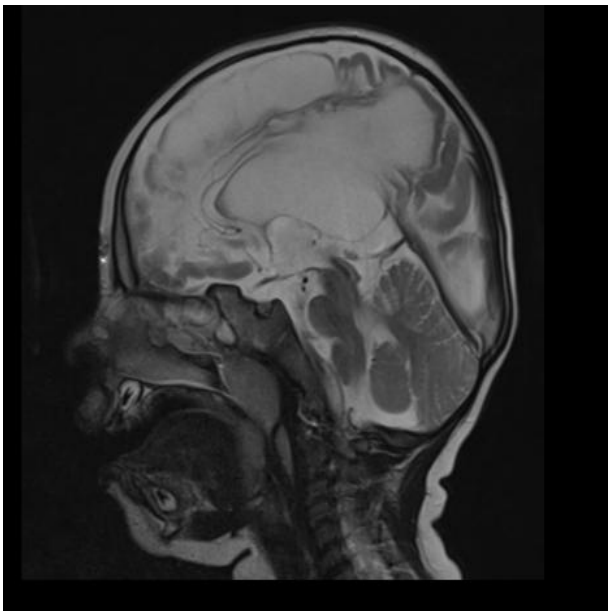
T2-AXIAL



FLAIR-AXIAL



T1-AXIAL



T2-SAGITTAL

Fig 17: CYSTIC ENCEPHALOMALACIA WITH THINNED OUT CORTEX IN BILATERAL FRONTO-PARIETAL REGION, SMALL & SHRUNKEN BASAL GANGLIA

ANNEXURE V: KEY TO MASTERCHART

AE	:	Antiepileptic
ATT	:	Anti-tubercular treatment
Cho	:	Choline
Cr	:	Creatine
FS	:	Focal seizure
D	:	Day
F	:	Female
GDD	:	Global developmental delay
GS	:	Generalized seizure
GTCS	:	Generalized tonic clonic seizure
M		Male
NAA	:	N Acetyl choline

ANNEXURE VI: MASTERCHART																						
Sl.	Age	Sex	MR No/Year	Seizure type	Duration	Conscious level	Others	Structural Malformation	Stroke	Infective	Hemorrhage	Encephalomalacia	Malformations, vascular	Atrophy	Mesial temporal sclerosis	Inborn Metabolic errors	Periventricular leukomalacia	Normal	MR diagnosis	Spectroscopy changes	Treatment	Results
1	7 DAYS	F	3553/18	GS	02 MINS	CONSCIOUS	-	-	+	-	-	-	-	-	-	-	-	-	SUBACUTE INFARCT IN THE CORTICAL AND SUBCORTICAL FRONTAL REGION, PARIETO-OCCIPITAL WATERSHED TERRITORY	↓NAA, ↑Lactate	AE	MAINTAINED
2	5 DAYS	M	3487/18	GS	05 MINS	CONSCIOUS	-	+	-	-	-	-	-	-	-	-	-	-	CORPUS CALLOSAL AGENESIS WITH COLPOCEPHALY	-	AE	MAINTAINED
3	2 MONTHS	F	7561/ 19	FS	1 MIN	CONSCIOUS	-	-	-	-	-	-	-	-	-	-	-	+	NORMAL	-	-	-
4	2 MONTHS	M	3072/18	FS	2 MINS	CONSCIOUS	-	-	-	-	-	-	-	-	-	-	-	+	NORMAL	-	-	-
5	1 YEAR	F	6627/19	FS	3 MINS	CONSCIOUS	EXCESSIVE CRY	-	-	-	-	-	-	-	-	-	-	+	NORMAL	-	-	-
6	4 MONTHS	M	7459/19	FS	02 MINS	CONSCIOUS	-	-	-	-	+	-	-	-	-	-	-	-	SUBDURAL HEMORRHAGE IN THE BILATERAL FRONTO-TEMPORO-	-	ANTI-COAGULANT THERAPY	IMPROVED
7	2 YEARS	M	6466/18	FS	30 SECONDS	CONSCIOUS	-	-	-	-	-	-	-	-	-	-	-	+	NORMAL	-	-	-
8	08 DAYS	F	3361/18	FS	02 MINS	CONSCIOUS	EXCESSIVE CRY	-	-	-	-	-	-	-	-	+	-	-	HYPOGLYCEMIC ENCEPHALOPATHY	↓NAA, ↑Lactate	IV GLUCOSE AND NICU CARE	IMPROVED
9	18 MONTHS	M	6262/18	FS	03 MINS	CONSCIOUS	-	-	-	-	-	-	-	-	-	-	-	+	NORMAL	-	-	-
10	1 YEAR	M	6728/18	FS	01 MIN	CONSCIOUS	-	-	-	-	-	-	-	+	-	-	-	-	DIFFUSE CEREBRAL ATROPHY	-	AE	MAINTAINED
11	6 DAYS	F	6575/18	GS	06 MINS	DROWSY	-	-	-	+	-	-	-	-	-	-	-	-	CEREBRAL ABSCESSES WITH EPENDYMITIS	↓NAA, ↓Cho-Cr ratio, ↑Lactate	ATT WITH AE	EXPIRED
12	2 MONTHS	M	6640/18	FS	02 MINS	CONSCIOUS	-	-	-	-	-	-	-	-	-	+	-	-	HYPOGLYCEMIC ENCEPHALOPATHY	↓NAA, ↑Lactate	IV GLUCOSE AND NICU CARE	IMPROVED
13	4 MONTHS	F	3594/18	FS	03 MINS	CONSCIOUS	-	-	-	-	-	-	-	-	-	-	-	+	NORMAL	-	-	-
14	15 DAYS	M	8563/19	FS TO GS	02 MINS	CONSCIOUS	-	-	-	-	-	-	-	-	-	+	-	-	MAPLE SYRUP URINE DISEASE	↑branched chain amino acids	AE	-
15	8 MONTHS	F	3457/18	FS	02 MINS	CONSCIOUS	-	-	-	-	-	-	-	-	-	-	-	+	NORMAL	-	-	-
16	11 MONTHS	M	3258/18	GS	03 MINS	DROWSY	-	-	-	-	-	-	-	-	-	+	-	-	MITOCHONDRIAL ENCEPHALOPATHY	↓NAA, ↓CHOLINE, ↑Lactate	AE	MAINTAINED
17	06 MONTHS	F	7405	UNKNOWN ONSET	02 MINS	CONSCIOUS	-	-	-	-	-	+	-	-	-	-	-	-	CYSTIC ENCEPHALOMALACIA IN THE RIGHT FRONTO-PARIETAL REGION	-	AE	MAINTAINED
18	01 YEAR	F	6627/18	FS	03 MINS	CONSCIOUS	-	-	-	-	-	-	-	-	-	-	-	-	NORMAL	-	-	-
19	06 MONTHS	M	7095/19	FS	02 MINS	CONSCIOUS	-	+	-	-	-	-	-	-	-	-	-	-	CORPUS CALLOSAL DYSGENESIS	-	AE	MAINTAINED
20	8 MONTHS	F	7624/19	FS	O5 MINS	UNCONSCIOUS	-	-	-	+	-	-	-	-	-	-	-	-	ACUTE NECROTIZING ENCEPHALITIS	↓NAA, ↑Lactate	AE	EXPIRED
21	2 YEARS	M	7882/19	FS	04 MINS	CONSCIOUS	EXCESSIVE CRY	+	-	-	-	-	-	-	-	-	-	-	RIGHT ANTERIOR TEMPORAL ARACHNOID CYST	-	AE	IMPROVED
22	20 MONTHS	F	7453/19	FS	03 MINS	CONSCIOUS	EXCESSIVE CRY	-	-	-	-	-	-	-	+	-	-	-	BILATERAL MESIAL TEMPORAL SCLEROSIS	↓NAA, ↓NAA/Cho	AE	MAINTAINED
23	12 MONTHS	M	3245/18	GS	01 MIN	CONSCIOUS	-	-	-	-	-	+	-	-	-	-	-	-	CYSTIC ENCEPHALOMALCIA WITH THINNED OUT CORTEX IN BILATERAL FRONTO-PARIETAL REGION, SMALL & SHRUNKEN BASAL GANGLIA	-	AE	MAINTAINED
24	4 months	F	6517/18	FS	02 MINS	CONSCIOUS	-	-	-	-	-	-	-	+	-	-	-	-	CEREBELLAR ATROPHY	-	AE	IMPROVED
25	22 MONTHS	M	6547/18	FS	O3 MINS	CONSCIOUS	GDD	+	-	-	-	-	-	-	-	-	-	-	LISSENCEPHALY TYPE I	-	AE	MAINTAINED
26	14 MONTHS	F	7346/19	FS	02 MINS	CONSCIOUS	-	-	-	-	-	-	+	-	-	-	-	-	ARTERIO-VENOUS MALFORMATION IN RIGHT FRONTO-TEMPORAL REGION	-	AE	MAINTAINED
27	16 MONTHS	M	6832 / 18	FS	01 MIN	CONSCIOUS	MICROCEPHALY	-	-	-	-	-	-	-	-	-	+	-	PERIVENTRICULAR LEUKOMALACIA	↓NAA, ↑Lactate	AE WITH OXYGEN SUPPORT	MAINTAINED
28	08 MONTHS	F	6796/18	UNKNO	02 MINS	CONSCIOUS	-	-	-	-	-	-	-	-	-	-	-	-	NORMAL	-	-	-
29	07 MONTHS	M	6264/18	FS	01 MINS	CONSCIOUS	-	-	-	-	-	-	-	-	-	-	-	-	NORMAL	-	-	-
30	13 MONTHS	M	7342/19	UNKNO	02 MINS	CONSCIOUS	-	-	-	-	-	-	-	-	-	-	-	-	NORMAL	-	-	-
31	19 MONTHS	F	6457/18	FS	03 MINS	CONSCIOUS	-	-	-	-	-	-	-	-	-	-	-	-	NORMAL	-	-	-