"MAGNETIC RESONANCE IMAGING EVALUATION OF ACUTE ENCEPHALITIS SYNDROME IN PEDIATRIC PATIENTS IN A TERTIARY CARE HOSPITAL – A CROSS SECTIONAL STUDY"

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LIST OF ABBREVIATIONS

GLOSSARY	ABBREVIATIONS
ADC	Apparent diffusion coefficient
ADEM	Acute disseminated encephalomyelitis
AES	Acute encephalitis syndrome
AIE	Autoimmune immune encephalitis
CFR	Case fatality rate
CSF	Cerebrospinal fluid
CT	Computerized tomography
DWI	Diffusion-weighted imaging
EBV	Epstein barr virus
ECD	Ethylene cysteine dimer
EEG	Electroencephalogram
ELISA	Enzyme linked immunosorbent assay
EPI	Echo planar imaging
FLAIR	Fluid attenuated inversion recovery
GABABR	Gamma-aminobutyric acid-b receptor
Gad	Gadolinium
HSV	Herpes simplex encephalitis
IgG	Immunoglobulin G
IgM	Immunoglobulin M
JE	Japanese encephalitis
JEV	Japanese encephalitis virus
LGI1	Leucine-rich glioma inactivated protein
MRI	Magnetic resonance imaging
MRS	Magnetic resonance imaging

NMDAR	N-methyl d-aspartate receptor
NS1	Non-structural protein 1
NVBDCP	National vector borne disease control programme
PCR	Polymerase chain reaction
RF	Radiofrequency
SD	Standard deviation
SN	Substantia nigra
SPECT	Single-photon emission computed tomography
SWI	Susceptibility weighted imaging
T1WI	T1-weighted images
T2 WI	T2-weighted images
TE	Time to echo
TR	Repetition time
WHO	World health organization

ABSTRACT

Background: Acute Encephalitis Syndrome (AES) is a multifactorial clinical entity, mostly caused by viruses. The etiology in a major number of AES cases still remains unclear. The season and geographical location seem to have an influence regarding the causative agents of AES, which predominantly affects pediatric age groups below 15 years. Magnetic Resonance Imaging (MRI) evaluation of the brain with the utilization of its basic and special MRI sequences gives a comprehensive understanding of various etiologies of AES. Hence, the present study was done to estimate the yield of MRI in patients suspected to have AES and to compare of various MRI sequences in AES patients.

Materials and methods: A hospital-based cross-sectional observational study was done on 68 subjects aged between 1 to 18 years with clinical features suggestive of AES attending the Radio-diagnosis department in a tertiary care institute. Various sequences of MRI were done with a 3.0 Tesla MRI scanner. T1 weighted image (T1WI), T2 weighted image (T2WI), Diffusion-Weighted Imaging (DWI), Fluid Attenuation Inversion Recovery (FLAIR), Susceptibility Weighted Imaging (SWI), Apparent Diffusion Coefficient, Magnetic Resonance Spectroscopy were the MRI sequences done. For all the tests, the value of p less than 5% (0.05) was considered significant. Data were analyzed by using SPSS software, V.22.

Results: Majority (42.65%) were aged between 1 to 6 years. The majority were males (63.24%). The yield of MRI was 61.76% (42 out of 68 subjects). Among the 42 subjects with MRI suggestive of AES, the radiological diagnosis supported infectious aetiology in 45.24% (n=19), para-infectious aetiology in 45.24% (n=19) and non-infectious aetiology in 9.52% (n=4). Among the basic sequences, the yield of T2 was better than T1. The yield of T2 was 100% for para-infectious and non-infectious AES.

It was 89.5% for infectious AES. With regards to special sequences, FLAIR was the most sensitive in picking up abnormalities. The yield of FLAIR was best (100%) for non-infectious and para-infectious AES. With regards to infectious AES, the yield was only 68.4%.

Conclusion: T2 WI was the most sensitive basic sequence while FLAIR was the most sensitive special sequence in clinically suspected patients undergoing MRI. Large-scale, multi-centric prospective studies in the future incorporating the evaluation of outcome and validity of MRI sequences in predicting the outcome are recommended.

Keywords: Acute Encephalitis Syndrome, Magnetic Resonance Imaging, Fluid Attenuation Inversion Recovery, Yield, etiology, para-infectious.

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INTRODUCTION:

Acute Encephalitis Syndrome (AES) is defined as an acute onset of fever with a change in mental status presenting as confusion or altered sensorium or coma or new onset of seizures (excluding febrile seizure).[1] AES is a multifactorial clinical entity, mostly caused by viruses. There have been increasing reports of bacteria, fungi, spirochetes, parasites, and chemicals causing Acute Encephalitis.[2] Viral encephalitis is one of the major causes of mortality and morbidity in the pediatric population. This group of diseases is further complicated by the various etiologies and lack of specific guidelines for evaluating and treating them. The incidence of AES is widely variable across various studies. The term "Acute Encephalitis Syndrome" was coined mainly for surveillance of Japanese Encephalitis. Any acute illness with pyrexia and altered mentation or convulsions or both come under this surveillance.[3]

As Japanese Encephalitis (JE) cannot be distinguished from encephalitis due to other causes based on clinical findings alone; there was a need for a systematic clinical approach. A suspected JE case is a person meeting the definition of AES. The mean incidence of JE is around 3.5 to 7.4 per one lakh patient-years, with the incidence typically higher among children.[4] Globally, JE is the major cause of AES. JE is endemic in 24 countries in South East Asian and Western Pacific regions, according to World Health Organization (WHO).[5] Case-fatality rate (CFR) in AES can be as high as 30%. In 30%–50% of those with AES, there can be permanent neurological deficits or psychiatric sequelae.[5] Around 50,000 cases are diagnosed per year, and 10,000 deaths result in every year in Asia due to JE in children aged below 15 years.[6]

The etiology in a major number of AES cases still remains unclear. The season and geographical location seem to have an influence regarding the causative agents of AES, which predominantly affects pediatric age groups below 15 years. According to the investigators, the causal agent for chemical encephalitis has been hypothesized to be a toxin prevalent in the litchi fruit seed, "methylene cyclopropyl glycine."

The complex and time-depleting process is the virological diagnosis of AES, besides being costly. Few agents have specific characteristic patterns on Magnetic resonance imaging (MRI) and electroencephalography, which can yield clues to specific diagnoses with the aid of laboratory investigations. Clinically, there is wide variation in the severity of the disease. A case severe enough would present with fever, convulsions, coma, neurologic deficits and ultimately result in death.

Neuroimaging plays an important role in the diagnosis and management of AES. The MRI findings in clinically suspected cases can be specific or non-specific, but their role in the etiological diagnosis of encephalitis is indispensable. MRI yields clues to the diagnosis of encephalitis aetiology as well as conditions which may mimic AES; and also highlights complications (such as mass effect, intracranial bleed); and also helps in prognosis.

MRI evaluation of the brain with the utilization of its basic and special MRI sequences gives a comprehensive understanding of various aetiologies of AES.[7] Time saving is MRI as it helps in early treatment administration and supportive care in the suspected cases. In patients with AE, the findings of Neuroimaging can be quiet different or normal. The MRI of the brain with and without contrast using T1-weighted, T2-weighted, diffusion-weighted imaging, susceptibility-weighted imaging, and fluid-attenuated inversion recovery (FLAIR) sequences is the modality of choice

in assessing the changes consistent with inflammation of brain parenchyma as specific MRI changes can be characteristically seen with a few pathogens.[8]

On MRI and CT, thalami, substantia nigra, basal ganglia, cerebral cortex, cerebellum, brain stem, and white matter are involved in Japanese encephalitis, whereas in Herpes simplex encephalitis (HSE), the frontal lobe, insula, cingulated gyri, and medial temporal lobe involvement is characteristic.[9] In such cases, the basal ganglia and thalami are almost always spared. In a study done at northeast India in 2021 showed that in JE, the majority had abnormal signal alterations in substantia nigra and bilateral thalami. It was concluded that Diffusion-weighted imaging and Apparent Diffusion Coefficient mapping were helpful in evaluating the stage of the JE. But significant differences between the pediatric JE and adult JE MRI features could not be established[15]. The most sensitive MRI sequences were FLAIR and T2 in revealing abnormalities in viral encephalitis.[7]

NEED OF THE STUDY:

There are only a few studies that have investigated systemically the aetiologies of AES with neuroimaging. Further research is important to delineate the relationship between results of neuroimaging and specific encephalitis aetiologies. The MRI findings can be specific or non-specific, but they have an important role in the etiological diagnosis of encephalitis. There is a lack of studies with regards to the usefulness and effectiveness of various conventional MRI sequences for evaluating AES.

Hence, the present study was done to estimate the yield of MRI in patients suspected to have AES and to compare of various MRI sequences in AES patients.

AIM AND OBJECTIVES:

1. To estimate the yield of MRI in the evaluation of patients suspected to have acute encephalitis syndrome.
2. To estimate the percentage of patients where MRI provided useful clues to definitive diagnosis and comparison of various MRI sequences in patients with acute encephalitis syndrome.

REVIEW OF LITERATURE:

ACUTE ENCEPHALITIS SYNDROME:

Definition:

Acute Encephalitis Syndrome (AES) is defined as "an acute onset of pyrexia associated with a change in mental status presenting as confusion or disorientation or coma or new onset of seizures (excluding febrile seizure)".[1]

The WHO in 2006 coined the term "acute encephalitis syndrome" (AES).

AES was coined specifically during the surveillance of JE. Any acute onset illness with pyrexia and altered sensorium or convulsions or both come under this surveillance.[3]

As JE cannot be differentiated from encephalitis due to other etiologies based on clinical findings alone, so there was a need for a comprehensive approach. A suspected JE case is a person meeting the definition of AES.

The AES clinical case definition is.[3]

"A person of any age at any time of year with the acute onset of pyrexia with least one of the following:

1. New onset of seizures (excluding simple febrile seizures).
2. A change in mental status (including symptoms such as confusion, inability to talk, disorientation or coma)."

AES is a multifactorial clinical condition, which is mainly caused by viruses. Even though there have been increasing reports of fungi, spirochetes, parasites, bacteria, and chemicals causing AES.[2] In the pediatric age group, viral encephalitis is a major cause of mortality and morbidity. Group of diseases in AES are further complicated by the varied etiology and lack of uniform specific guidelines for evaluating and treating them.

Epidemiology:

The epidemiology of AES is difficult to calculate because of the paucity in uniform standardized definitions across the continents and study populations.

1. **Global:**

The average incidence is around 3.5 to 7.4 per one lakh patient-years, with the incidence especially being more among children.[4] World wide, JE is considered the major cause of AES. Japan was the first country where JE was first recognized in 1924. The epidemics in Japan and China have gradually come down since the late 1960s, after which JE has spread to new grounds.[10] According to World Health Organization (WHO), JE is endemic in 24 countries in South East Asian and Western Pacific regions. [5] In 2019, worldwide, 68000 clinical cases of JE per annum were estimated to occur, and most were to occur in the South-East Asian and western pacific region. The risk of infection was estimated to be more than 3 billion. Per year around 50,000 cases occur, with 10,000 deaths per annum in Asia due to JE in age group below 15 years.[6]

2. India:

In India, AES diagnosed clinically due to Japanese Encephalitis Virus (JEV) in 1955 in Tamil Nadu for the first time.[11-13] JEV is the major cause of viral AES in India (5%-35%). "Dengue, Parvovirus B4, enteroviruses, Epstein-Barr virus, herpes simplex virus, Influenza A virus, West Nile virus, Chandipura virus, mumps, measles, and scrub typhus, S.pneumoniae are the other causes of AES among the sporadic and outbreak cases from India". [11] Other causative agents for AES were Nipah virus and Zika virus. 10,485 AES cases, including 632 deaths from 17 states, were reported to the "National Vector Borne Diseases Control Programme" (NVBDCP) in India in 2018. The CFR was approximately 6 percent.[11] Kamble S et al.[14] (2016) in their case series of 36 AES cases in Bellary district, observed that majority were toddlers (30.1%) and pre-school children (26.5%). Male children were affected in 64.7% of cases, and 58.8% of children from the rural area were infected. The post-monsoon period was the time where the majority of cases were detected (45.1%), followed by the monsoon period (30.1%). Of all the cases, 84.5% were suspected of having viral etiology. The attack rate is higher in children because of the absence of cumulative immunity that results from natural infections. Approximately 25% of children affected died from the disease, and among those which survived, physical and mental impairment was evident in 30%–40% of cases.[15]

Tiwari JK et al.[16] in their study on 3088 patients, observed that 22.7% tested positive for one or more viruses. The most common viral etiologies were HSV (8.45%), EBV (5.6%). It was concluded depending on the season, testing for arboviruses should be done.

Etiology and Pathogenesis of AES:

Etiology can be broadly classified as infective (bacteria and viruses) or non-infective.[17]

The etiology in a large number of AES cases still remains unidentified. Worldwide, JE is the major cause of AES. Due to a large number of agents capable of causing encephalitis, etiologic diagnosis is complex.[8]

The virus or the causative agent may be demonstrable only in the brain and can be either absent or temporarily found in fluids such as cerebrospinal fluid (CSF) or blood.

The Virological diagnosis of AES is complicated, costly, and is time-consuming. Hence based on the local etiological scenarios, management should be done.

"Etiology of acute encephalitis syndrome[8, 18]

I. Viral agents that are known to cause encephalitis:

A. Arboviruses, togaviruses, and alphaviruses

- Western equine encephalitis virus
- Eastern equine encephalitis virus
- Venezuelan equine encephalitis virus

B. Flaviviruses (mosquito-borne)

- Japanese encephalitis virus
- St Louis encephalitis virus
- West Nile virus

- Murray Valley encephalitis virus
- non-arthropod-borne togavirus – rubella virus

C. Bunyaviruses

- California encephalitis virus

D. Reoviruses

- Colorado tick fever encephalitis virus

E. Herpesviruses

- Herpes simplex 1 and 2
- Varicella zoster virus
- Epstein–Barr virus
- Cytomegalovirus
- Human herpesvirus – 6
- B virus

F. Enteroviruses

- Polioviruses
- Coxsackie viruses
- Echoviruses
- Enteroviruses 70 and 71

G. Orthomyxoviruses

- Influenza viruses

H. Paramyxoviruses

- Measlesvirus
- Mumpsvirus
- Parainfluenza viruses
- Nipah virus

I. Adenoviruses

J. Parvoviruses

K. Rhabdoviruses

II. Non-viral agents

A. Rickettsia: Rocky Mountain spotted fever, endemic and epidemic typhus, Coxiella burnetti, Ehrlichiosis, scrub typhus

B. Bacterial:

○ Pyogenic (bacterial) meningitis

○ Tuberculousmeningitis

○ Mycoplasma pneumoniae

○ Listeria monocytogenes

○ Spirochetes: syphilis, Leptospirosis,

○ Lyme disease

○ Brucellosis

○ Legionella

○ Salmonella typhi

○ Cat scratch disease (Bartonellosis)

C. Fungi: Cryptococcus, histoplasma, aspergillus, mucormycosis, candida, coccidiomycosis

D. Protozoa: naeglaria, acanthameba, *Toxoplasma gondii*

E. Metazoa: Trichinosis, echinococcus, cysticercus, schistosoma

III. Non-infectious inflammation of brain

- Acute disseminated encephalomyelitis
- Antibody-associated encephalitis
- Collagen vascular disorders

IV. Infectious encephalopathy

- Cerebral malaria
- Shigella encephalopathy
- Dengue encephalopathy
- Sepsis syndrome
- Enteric encephalopathy

V. Structural causes of coma with associated fever due to another cause

- Tumor
- Vascular event
- Head injury
- Other space occupying lesion

VI. Functional causes of coma with associated fever due to another cause

- Electrolyte encephalopathy
- Reye's syndrome
- Diabetic coma
- Uremic coma
- Hepatic coma
- Inborn error of metabolism
- Chemicals
- Toxins
- Hypertensive encephalopathy

Encephalitis may be

i. Infectious, caused due to direct invasion of the brain. It is most commonly due to the involvement of gray matter by the pathogen, or

ii. Immune-mediated, involving white matter commonly.

Both neurotropic and non-neurotropic pathogens can cause encephalitis. Neurotropic viruses like arboviruses, after viraemia, can cross the blood-brain barrier. They could also enter the brain through retrograde axonal transport, like in the case of the rabies virus.[8] Neuronal infection can result in cytokine release leading to cytotoxicity, inflammation, and tissue damage.[19] In the case of varicella-zoster virus infection, vasculitis can occur, leading to tissue ischemia.[20]

AES in India:

After the reporting of the first case from Tamilnadu in 1955, the report of the first outbreak came from Bankura district, West Bengal, in 1973.[11-13] The CFR is high in JE is high and even in those who survive, it can cause neurological sequelae such as "convulsions, episodic headache, autonomic disturbance, abnormal behaviour, mood disorder, intellectual deficit, paresis, incoordination of movements, jerky limb movements, speech disorder, cranial nerve palsy, gaze palsy, parkinsonian features, impaired hearing, etc."[21]

Joshi R et al.[2] classified AES history in India into three phases: "(a) Before 1975 when a few cases with aetiology of JE were identified; (b) Between 1975 to 1999, more cases were reported with frequent outbreaks resulting in JE endemic regions (Tamil Nadu, near Gangetic plains and parts of Deccan) (c) between 2000 and 2010, there was an increase in non-JE outbreaks (Chandipura virus, Nipah virus and other enteroviruses)."

Clinical presentation:

The Clinical presentation depends on the involvement of the brain parenchyma or meninges. But a causative agent can have a meningitis presentation in one group

and encephalitic presentation in another group.[22] In children, the typical symptoms could be fever with headache and vomiting initially for a week followed by symptoms/signs of neurological deficits and/or meningeal irritation. Older children more commonly report headaches compared to young children. The severity can vary from a febrile illness which is mild in nature with a headache, to a more severe disorder presenting with neurological deficits, convulsions, coma, or even death. The onset of the disease is usually sudden, with fever accompanied by declining mental status. This could be accompanied by agitation, irritability, spells of screaming, confusion, drowsiness, delirium, stupor, and/or coma. In severe cases, there can be life-threatening problems like an increase in intracranial pressure or flaccid coma. It could last for 7 to 10 days. The recovery is steady after this stage with or without a sequel.[8, 18]

Clinical History, Examination, and Diagnosis:

Skin rash is seen in conditions such as measles, enteroviral encephalitis, dengue, rickettsiae, and varicella-zoster. In Rabies, there will be characteristic hydrophobia. In influenza, teher can be concurrent infection of the upper respiratory tract.

Neurologic signs cannot identify the underlying etiology with reliability. Depending on the region involved, the presentation can be characterized. In Uttar Pradesh, two different clinical syndromes have been identified for infectious AES. “Pure neurologic illness like JE and HSV encephalitis, while the other is a multisystem syndrome compromising of rash, hepatosplenomegaly, bleeding seen in infections such as dengue, leptospirosis, enteric fever and cerebral malaria.”[23]

In Antibody-associated or autoimmune encephalitis, IE, the manifestations are predominantly psychiatric in the early course of the disease like psychosis, compulsive behaviors, etc. Cognitive decline, seizures, and coma are also common. Also, these psychiatric manifestations with extrapyramidal movements can occur in both types of encephalitis. Hence there arises the need for imaging and other investigations for confirming the etiology.

Diagnosis:

The battery of diagnostic tests includes lumbar puncture, MRI of the Brain, and Electroencephalogram in all cases suspected to have encephalitis. CSF is collected for analysis after ruling out contraindications for lumbar puncture. In viral encephalitis, CSF has a predominantly lymphocytic mononuclear pleocytosis (but can also be neutrophilic in the initial course of the disease). The CSF has normal glucose and increased protein pattern in Viral encephalitis.[24-26]

In India, the NVBDCP has set up surveillance throughout the country for AES through sentinel sites. The main focus is on JE in India**.** IgM Capture ELISA is used for diagnosis of AES/JE.[15] Isolation of the virus is done at National Reference Laboratory.[11, 15]

"A Laboratory-Confirmed case of AES is a suspected case which is positive for any one of the following:

1. Isolation of virus from the brain tissue.
2. Presence of IgM antibody in serum and/ or CSF to a specific virus including JE/Entero Virus or others.
3. The four-fold difference in lgG antibody titre in paired sera.

4. Antigen detection by immunofluorescence.
5. Nucleic acid detection by PCR".

Virological diagnosis is costly, more complex, and involves a lot of time. In many cases, the virus is detected in the brain only and can be absent or only transiently found in CSF or Blood. It is difficult to reach an etiological diagnosis, even in well-equipped centres, in the majority of the cases.[27] The time of collection of the sample that is CSF or Blood also plays a role. PCR usually is helpful in the initial stages of illness, while IgM takes about 4 to 7 days for appearance. For diagnosis of AES/JE, IgM capture ELISA in CSF is used. Although PCR for JE in CSF/Serum confirms the diagnosis, the rate of positivity is highly variable.[8, 28, 29] For diagnosis of dengue and associated encephalitis, serum IgM and NS1 antigen detection are used. Serum ELISA IgM is used for diagnosing meningoencephalitis associated with scrub typhus. Detection of autoantibodies in CSF/serum confirms Autoimmune encephalitis. But the specific etiology remains unknown in the majority of the cases. EEG can also be used for localizing signs, for detecting subclinical seizure activity and encephalopathy. In about 1/3rd of subjects with Herpes Simplex Viral Encephalitis, "periodic localizing epileptiform discharges are seen."[30] In Autoimmune encephalitis, an extreme delta brush pattern is seen.[31] Neuroimaging plays an important role in AES diagnosis.

Role of MRI in Acute Encephalopathy Syndrome:

Evaluation with MRI Brain in different sequences can give comprehension and understanding of various etiologies of AES.[7] MRI is time-saving as it helps in starting treatment early and supportive to the confirmatory

diagnosis. In AES, finings in MRI can be quiet different or can be normal. Specific MRI changes can be seen with a few pathogens.[8]

On MRI and CT, JE involves "thalami, substantia nigra, basal ganglia, cerebral cortex, cerebellum, brain stem, and white matter." In Herpes simplex viral encephalitis, the temporal and frontal lobes are classically affected.[9] "Bilateral temporal and perisylvian hyperintense signal abnormality extending into the cingulate gyrus, typical of HSV encephalitis" was seen in a reported case study.[32] Thalamic involvement can also be seen.

JE causes T2 hyperintensities in the thalami, basal ganglia, and brain stem.[33] In JE, in a small proportion of subjects, temporal lobe changes are seen.[34, 35] "The temporal lobe involvement pattern is fairly characteristic and mostly involves the hippocampus, usually sparing the rest of the temporal lobe. This and the concurrent involvement of the thalami, substantia nigra (SN), and basal ganglia allow differentiation from HSE".[34, 35] Recognizing characteristic findings within limbic structures can alert clinicians to the potential diagnosis. Phukan P et al.[36] in their study, observed that in JE, the majority had signal alterations in substantia nigra and bilateral thalami. They concluded that DWI with Apparent Diffusion Coefficient mapping can help in evaluating the JE stage. But they did not observe significant differences between MRI features in adult and pediatric JE.

In autoimmune or paraneoplastic limbic encephalitis, "an increased signal intensity has been observed in the medial temporal lobes, and it is associated with antibodies against the gamma-aminobutyric acid-B receptor (GABABR) or leucine-rich glioma inactivated protein 1 (LGI1)".[37] In 60% of patients with anti-NMDAR encephalitis, the MRI of the brain seems to be normal.[38]

MRI SEQUENCES – BASICS AND DIFFERENCES:

MRI is the best imaging modality for imaging of the brain and spine. The quality of the images depends on several technical factors like the positioning of the patient, proper coil selection, selection of appropriate sequences, and image planes. MRI has the advantage of visualizing anatomy in all three planes: axial, sagittal, and coronal. MRI is based on the magnetization properties of atomic nuclei. The various types of images are produced by altering the sequence of Radio Frequency pulses applied and collected. "Repetition Time (TR) is the amount of time between successive pulse sequences applied to the same slice," while "Time to Echo (TE) is the time between delivery of the RF pulse and receipt of the echo signal." The various MRI sequences used in this study are

1. T1 weighted image
2. T2 weighted image
3. Diffusion-Weighted Imaging
4. Fluid Attenuation Inversion Recovery
5. Susceptibility Weighted Imaging
6. Apparent Diffusion Coefficient
7. Magnetic Resonance Spectroscopy.

Two different relaxation times characterize the tissues. They are T1 and T2.

T1 (longitudinal relaxation time) is "the time constant which determines the rate at which excited protons return to equilibrium. It is a measure of the time taken for spinning protons to realign with the external magnetic field".

T2 (transverse relaxation time) is "the time constant which determines the rate at which excited protons reach equilibrium or go out of phase with each other. It is a measure of the time taken for spinning protons to lose phase coherence among the nuclei spinning perpendicular to the main field".

Figure 1: **T1 weighted image**

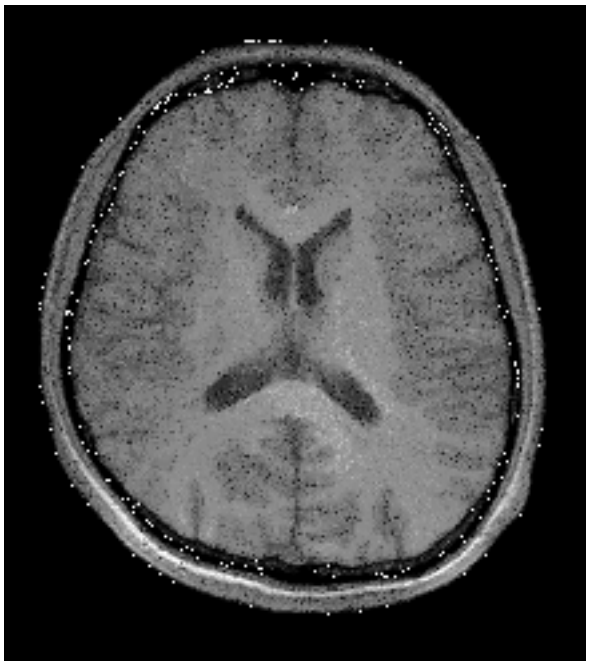
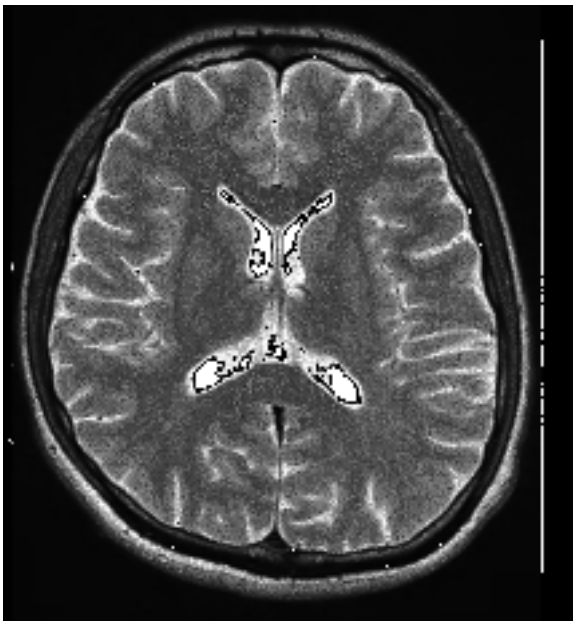


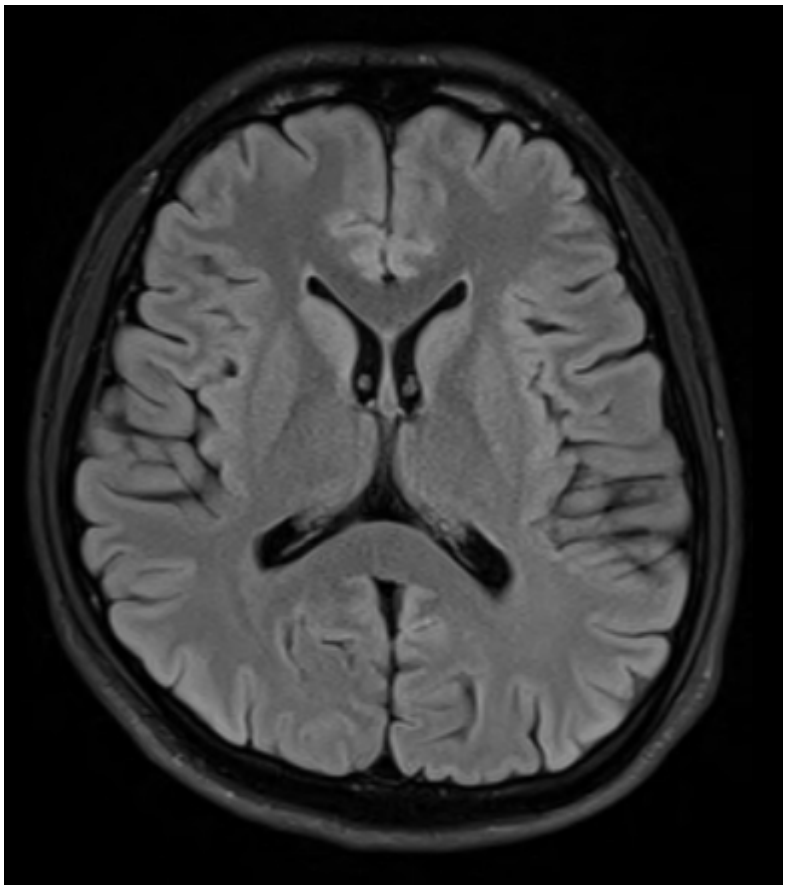
Figure 2: T2 Weighted image.



T1-weighted (T1W) and T2-weighted (T2W) scans are the most commonly used images. T1W images are created by using short Time to Echo (TE) and Repetition Time (TR). T2W images are created by using long TE and TR. They can be distinguished by seeing the CSF, which is bright on T2WI and dark on T1WI.

Fluid Attenuated Inversion Recovery (FLAIR) is similar to a T2WI except for the long TE and TR. Here the abnormalities look bright while CSF is attenuated and dark. It has the ability to pick up the pathologies very sensitively.

Figure 3: FLAIR image sequence.



Non-toxic **Contrast** enhancing drugs such as **Gadolinium (Gad)** can also be used in T1WI. There is a shortening of T1 with an injection of contrast and hence appears very bright on T1WI. They are helpful in evaluating vascular structures and blood-brain barrier breakdown.

Diffusion-weighted imaging (DWI) can sense random movements of water protons, also known as diffusion. In extracellular space, water molecules move freely. In ischemia of the brain tissue, there is the shutdown of the sodium-potassium pump, and it results in the accumulation of sodium intracellular. This restriction of intracellular water movement can be visualized in SWI as an extremely bright signal. Hence, DWI is very sensitive in picking conditions such as acute stroke.

How do we acquire diffusion-weighted images? The basic sequence is called "Stesjkal-Tanner pulsed gradient spin echo sequence and is a spin-echo sequence with diffusion gradients applied before and after 180-degree pulse". Diffusion sequences in present use are diffusion gradients applied to echoplanar (EPI) sequence with infinite T2.

Figure 4: DWI brain images using 3 different b values (0, 500, and 1000 s/mm^2)

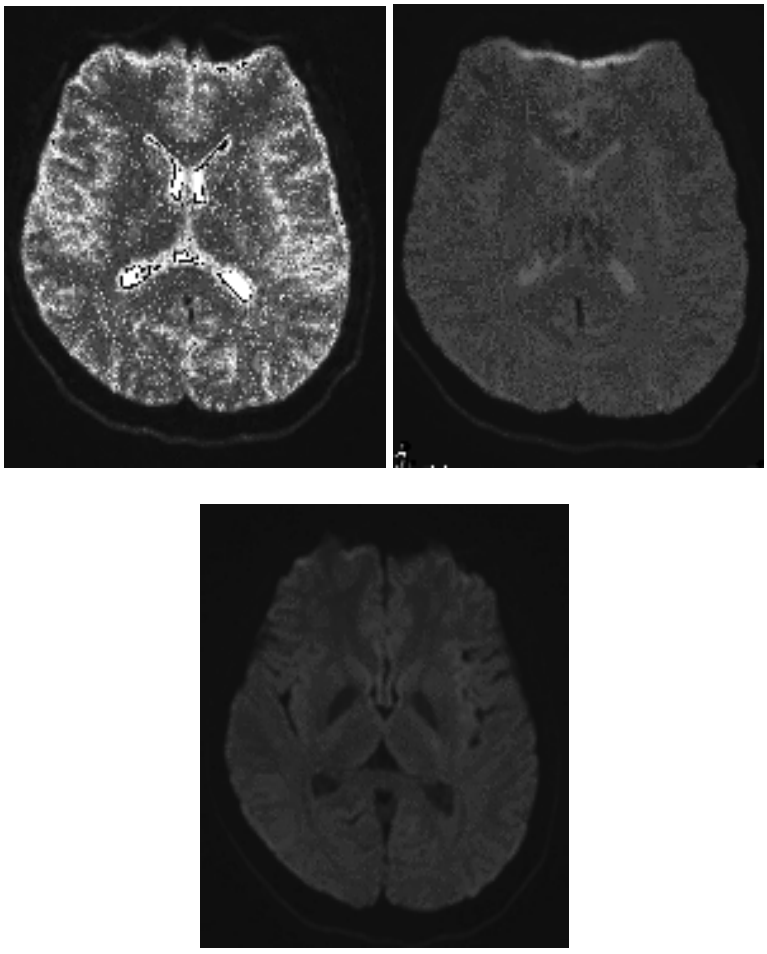
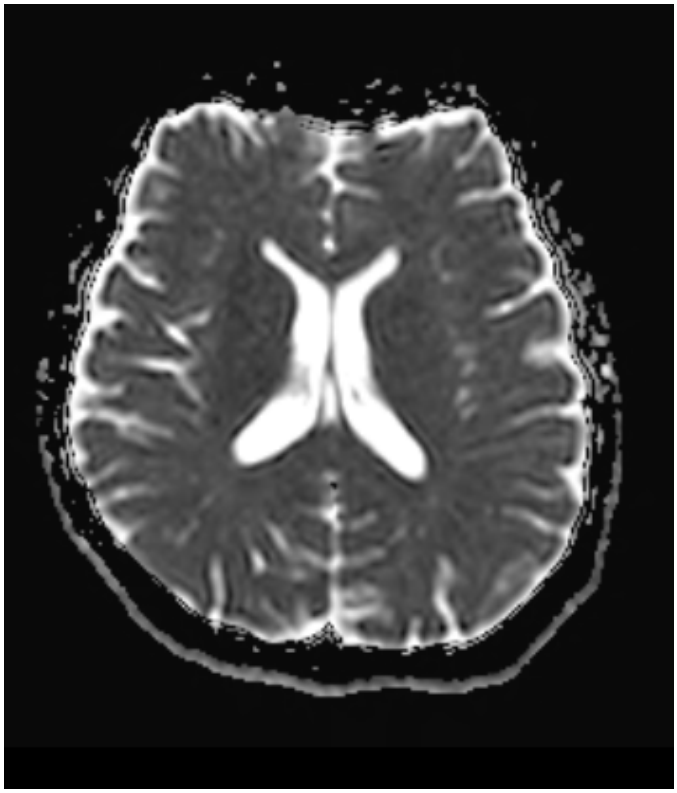


Figure 5: ADC sequence.



MR Spectroscopy (MRS):

This sequence uses magnetic resonance to access various biological metabolites from the body tissues non-invasively, which is then used to diagnose diseases, monitoring the diseases, and assessing response to the treatment.[39, 40] Chemical shift is the basis of MRS, while it is one of the causes of artifacts in MRI.

MR images are reconstructed from the entire proton signal from the tissue dominated by water and fat proton signals. Metabolite signals of clinical interest resonate between resonant frequencies of water and fat. Chemical shift is expressed in parts per million (ppm), which will be the same for a particular metabolite at all field strengths.

In a homogeneous field, the frequency of protons in given metabolites is equal to the chemical shift = position of metabolite peak.

Figure 6: VOI with Grid. Blue-voxel, white-volume of interest from which data is acquired and green-grid to prevent lipid contamination from the scalp interfering with signals.

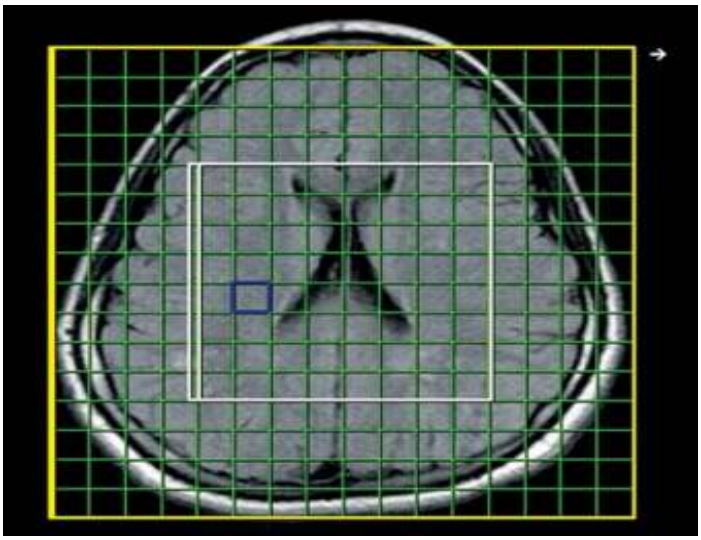


Figure 7: Three planes localization of the voxel and VOI. Note the position of the voxel in all three planes.

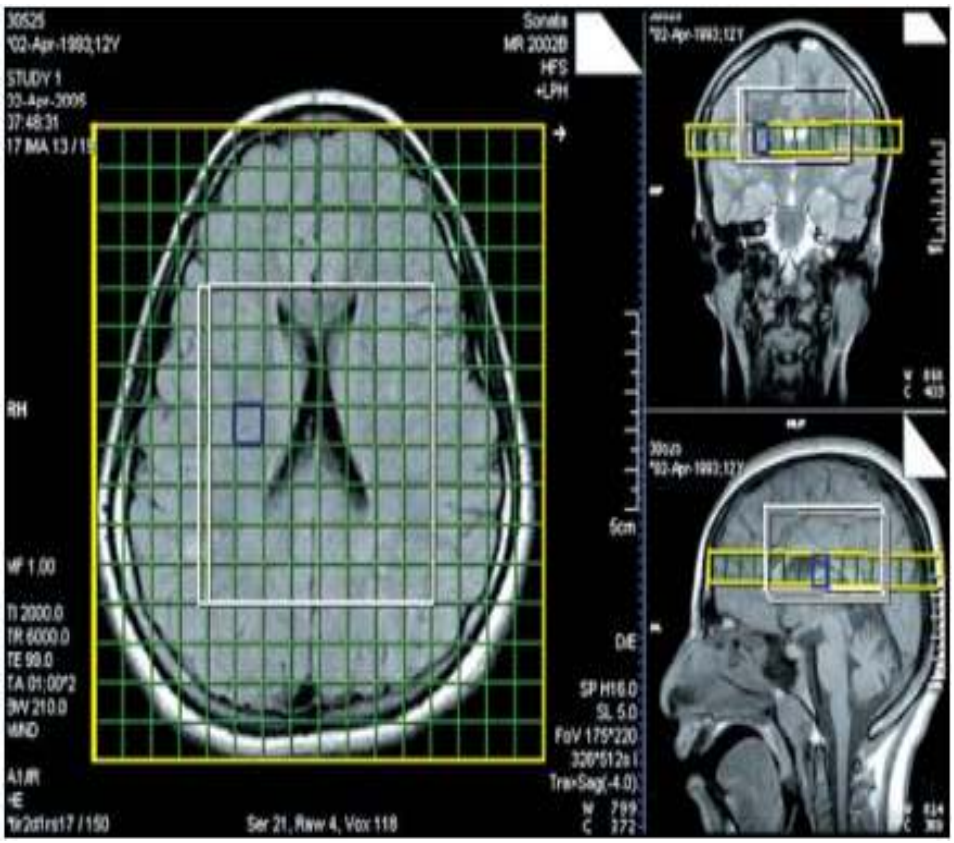
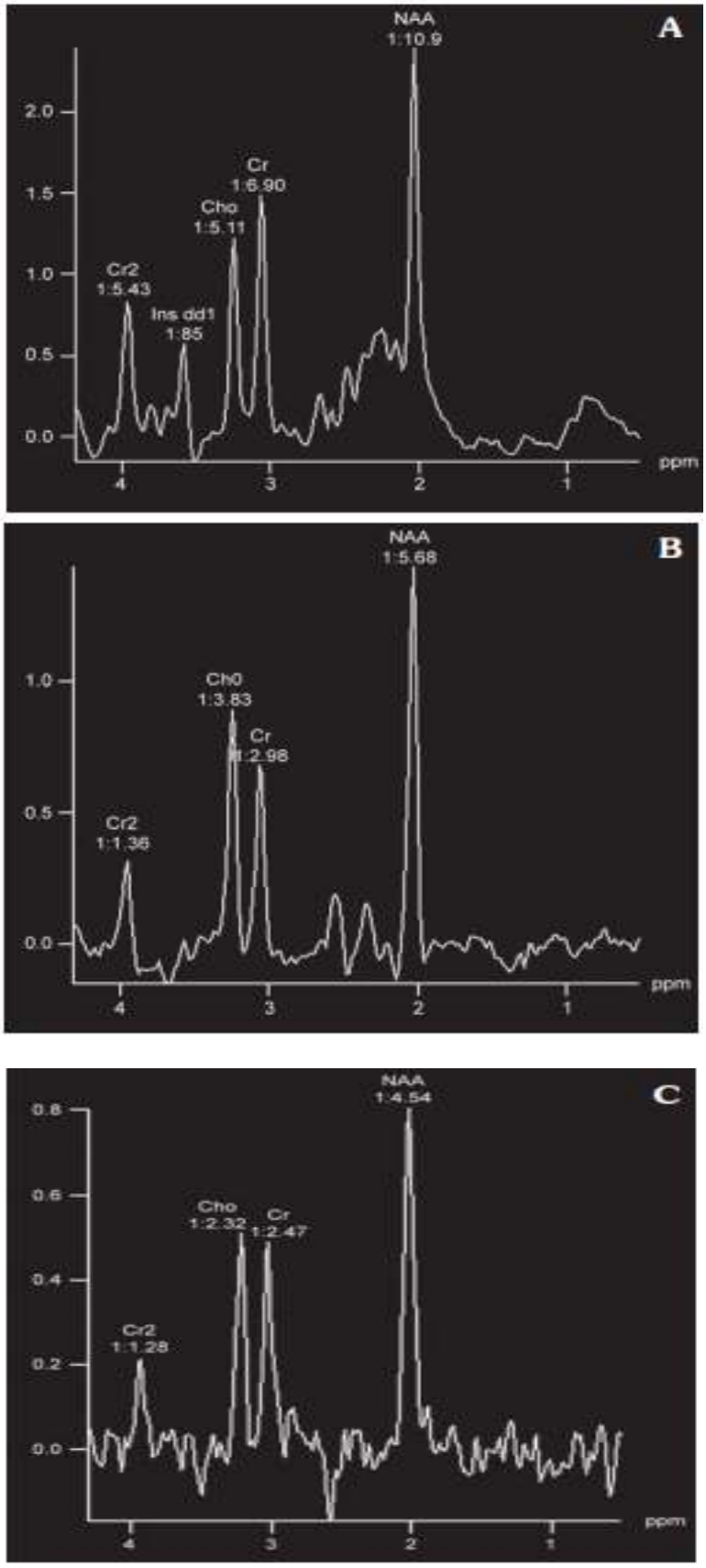


Figure 8: A to C: Normal spectra at 30 (A), 135 (B), and 270 ms (C).



Susceptibility weighted imaging (SWI):

It is a sequence that can detect the compounds capable of distorting the local magnetic field. Blood products are capable of distorting the local magnetic field and hence change in the signal because of paramagnetic, diamagnetic, and ferromagnetic properties.

Typically, the images presented are:

1. Magnitude.
2. Filtered phase.
3. SWI (combined post-processed magnitude and phase).

Figure 9: SWI Mag image.

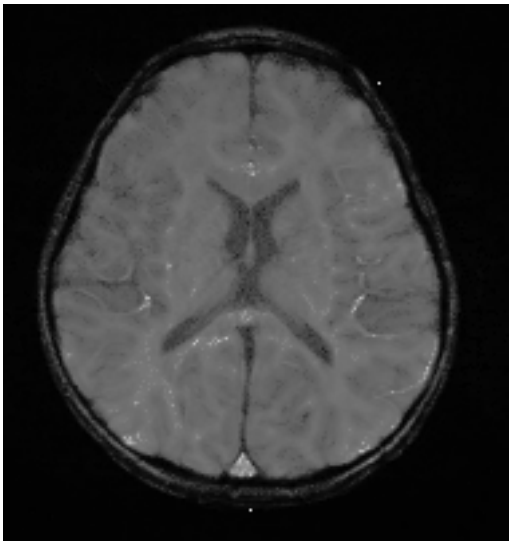


Figure 10: SWI Phase contrast.

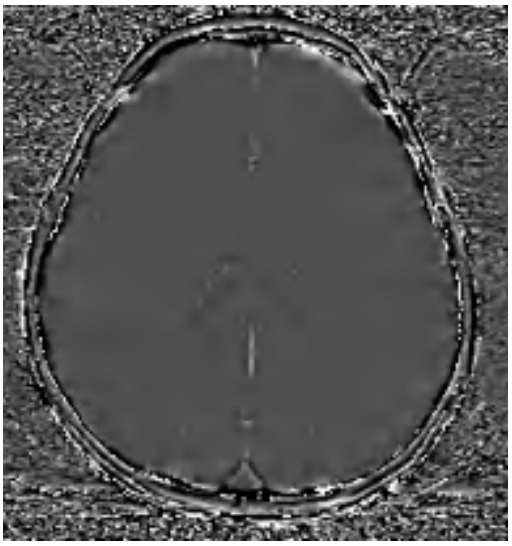


Figure 11: SWI mip images.

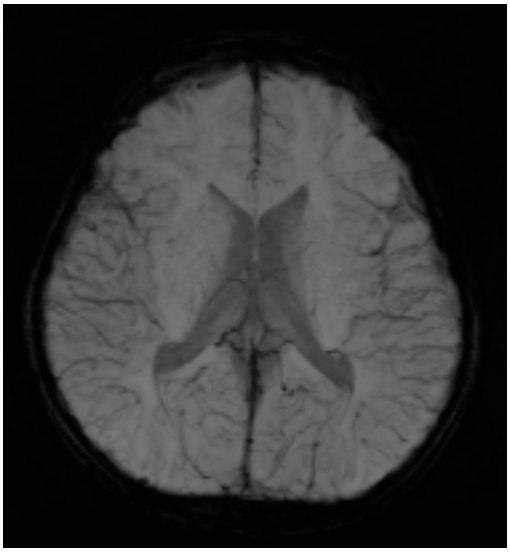
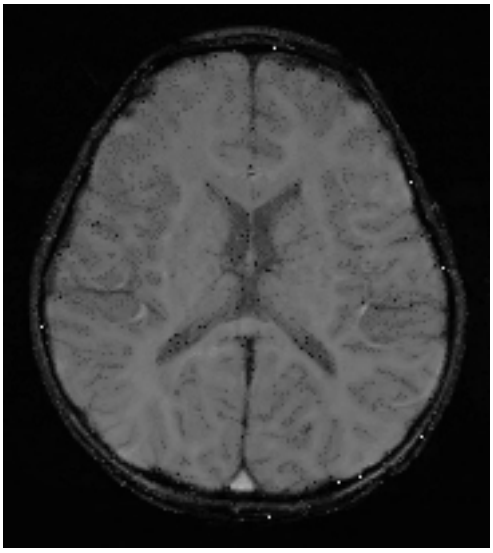


Figure 12: SWI image proper.



Contraindications to MRI include the presence of implanted magnetic, electronic devices, and other metallic devices like pacemakers, artificial heart valves, and intraocular metallic foreign bodies. Pregnancy is a relative contraindication due to unknown effects on the fetus.

MRI sequences also have some disadvantages. They are Subject to motion artifacts and require prolonged acquisition time for many images. They are inferior to CT in detecting acute hemorrhage and bony injuries.

Most Relevant studies:

Phukan P et al.[36] (2021) did a cross-sectional study on 54 JE subjects who were positive serologically in Northeast India with symptoms of Acute encephalitis. "54 JE patients (31 males and 23 females) having 32 pediatric and 22 adult JE constituted the study sample. Group 1 JE (*n* = 16) had encephalitic symptoms for less than 15 days, and group 2 JE (*n* = 38) had symptoms more than 15 days. Group 1 JE had mean apparent diffusion coefficient (ADC) value of 0.563 ± 0.109 (standard deviation [SD]) × 10^{-3} mm^2 /sec and group 2 JE had 1.095 ± 0.206 (SD) × 10^{-3} mm^2 /sec. The mean ADC value of pediatric JE was 0.907 ± 0.336 (SD) × 10^{-3} mm^2 /sec and adult JE was 0.982 ± 0.253 (SD) × 10^{-3} mm^2 /sec. They concluded that in JE, the majority of subjects show abnormal signal alterations in bilateral thalami and substantia nigra. Diffusion-weighted imaging with ADC mapping helps in evaluating the stage of the JE". They concluded that there was no significant difference statistically between adult and pediatric JE with respect to MRI findings.

Tripathy SK et al.[17] (2019) in their observational study, evaluated 834 children aged between 5 to 15 years with viral acute encephalitis syndrome. "In neuroimaging, with HSV-I infection, the majority had high-intensity lesion in the temporal lobe on T2-weighted images while the rest had high-intensity lesion both on temporal areas and frontoparietal areas. They also rarely had high-intensity lesions globally or on the limbic area. The global involvement was more common compared to the temporal lobe in HSV-II infection. In JE, limbic area involvement was more common compared to global cerebral involvement". They concluded that only global involvement was seen in varicella-zoster virus infection.

Ghosh MK et al.[41] (2018) in their study, investigated the prognostic significance of clinical & radiological features of AES. They did a hospital-based prospective study on 628 subjects. Common radiological findings included basal ganglia involvement (16.1%), cortical involvement (14.5%), white matter involvement (13.1%) & diffusion restriction (12.6%). Cerebellar involvement was least common (1.3%). The mean age of the study population is 5.3±2.1 years & 62.1% of them were boys. Clinical features includes fever between 100-102° F (76.0%) & convulsions of <2 episodes (48.1%). altered consciousness (46.5%), cranial nerve palsy (16.2 %), motor weakness (11.3 %) & tone disturbance (19.7 %) & bleeding manifestations (9.7%). Common radiological findings included basal ganglia involvement (16.1%), cortical involvement (14.5%), white matter involvement (13.1%) & diffusion restriction (12.6%). Cerebellar involvement was least common (1.3%). The bleeding manifestation was the worst prognostic indicator (Adjusted odds ratio-43.9).

Pandit N et al.[42] (2018) in their observational study, performed MRI Brain on 19 children aged between 0 to 15 years age diagnosed with JE by IgM ELISA in the early course of illness. Thalamic involvement was most common, while insular involvement was least common. The basal ganglia, brainstem, cerebellum, and temporal lobe were the other areas involved. There was a restriction in DWI images. The hyperintensity in T2/FLAIR images was less marked on comparison with DWI images.

James J et al.[43] (2018) evaluated a single case of herpes simplex encephalitis with normal CSF analysis. MRI brain revealed “T2 and fluid-attenuated inversion recovery hyperintensities in the bilateral insular cortex, cingulate gyrus, medial

temporal lobes and the orbitofrontal gyrus of both the frontal lobes with diffusion restriction, typical of herpes simplex encephalitis". They concluded that hyperintensity in the inferior frontal and medial temporal lobe with a normal CSF and EEG findings, which are not specific, in their case was diagnostic of herpes simplex encephalitis.

Jain P et al.[44] (2017) in their cross-sectional study on 4092 subjects, observed JE (8%) and Dengue virus (8%) to be the most common aetiological agents for AES. JE, Dengue, and scrub typhus are the main aetiologies in Uttarpradesh. Sporadic cases are caused by Enteroviruses, herpes viruses, and bacteria. Adults are also becoming equally affected compared to children recently. In monsoon and post-monsoon seasons, there is an increasing prevalence of non-viral AES. They also stressed the need for MRI as etiology could not be traced in the majority of cases.

Jayaraman K et al.[45] (2018) in their review article, observed that "Encephalitis can involve any age group from children to old people. They observed that severity of the disease depends on the viral agent and the host immune system". They concluded that MRI findings can play an important role in evaluating encephalitis diagnosis and its etiology.

Bykowski J et al.[46] (2015) in their study on 141 patients with AES (2005 to 2012), observed that 50% had abnormal MRI findings. They observed that in children with abnormal MRI, there was a longer hospital stay. Acute brain MRI was done in 134 children and post-contrast imaging in 126 children. They observed Meningeal enhancement in 26 children. In 36%, DWI lesions were associated with the basal ganglia. On FLAIR, all diffusion-restricted lesions were evident. In 3 children, there was a normal acute MRI, but it became abnormal subsequently within a week.

Songmen S et al.[47] (2015) studied "the pattern of brain involvement in MRI in patients with acute encephalitis syndrome and to correlate the findings with clinical and laboratory data. Methods: The study was a retrospective hospital record-based review conducted at Tribhuvan University Teaching Hospital. MRI and records of patients undergoing MRI for acute encephalitis syndrome during two years duration were studied. Data analysis was done using IBM SPSS 20.0. A total of 47 MRI were studied, among which 11(23.40%) were pediatric, and 36(76.59%) were adult population. Edema was the commonest manifestation. The cerebral hemisphere (temporal lobe) was the commonest location involved 34(72.3%). Basal ganglia and thalamus involvement were also fairly common. Five (26.31%) out of 19 patients had positive Japanese encephalitis, 5(26.31%) had HSV antigen-positive serology, and in 8(42.10%), no etiology could be found. Posterior fossa and basal ganglia involvement were the most predominant findings in Japanese encephalitis, and involvement of the medial temporal lobe was seen in all cases of Herpes encephalitis. Fifteen patients had a good prognosis: complete recovery or minimal residual deficit, while four patients were either dead or left against medical advice. They concluded that medial temporal lobe involvement was seen in all cases of Herpes encephalitis, and thalamus and basal ganglia involvement was a predominant pattern in Japanese encephalitis. Posterior fossa involvement was common probably due to a non-conventional etiological agent".

Rozenberg F et al.[48] (2013) in their review on Acute viral encephalitis, observed that HSV is the commonest cause in western countries for encephalitis. The sequel is high despite antiviral therapy. Because of HSV latency, relapses can occur.

Misra UK et al.[7] (2010) in their study on 88 acute viral encephalitis patients aged between 2-72 years, evaluated the role of various MRI sequences. "Using ELISA or PCR, Serum or CSF was analyzed for dengue, JE, herpes, measles, echo, coxsackie, and polio viruses. Cranial MRI was done, and T1, T2, FLAIR, and DW images were obtained. The changes in MRI correlated with the type of encephalitis and duration of illness. All the patients had altered sensorium, and 37 had seizures. 22 patients had JE, 9 had dengue, 8 had herpes simplex encephalitis (HSE), 2 had Epstein-Barr virus encephalitis (EBVE), and 47 had non-specific encephalitis. The median duration of the MRI study from the onset was 10 days. In JE (20/22), HSE (8/8), and EBVE (2/2), MRI abnormalities were more common compared to dengue (2/9) and non-specific (20/47) encephalitis. The MRI abnormalities were more common in FLAIR (57.1%) compared to T2 (52.9%), DWI (38.1%), and T1 (19.3%) sequences. The mean ADC value in JE patients was lower ($974.0\pm110.85\times10^{-6}$ mm^2/s) than HSE ($1024.33\pm485.76\times10^{-6}$ mm^2/s). Additional MRI lesions were seen in 12.6% of cases on the FLAIR sequence. FLAIR and T2 sequences were more sensitive in revealing abnormalities in viral encephalitis".

Granerod J et al.[4] (2007) in their study, assessed "the role of imaging in the early management of encephalitis. 101 MRIs from 80 subjects and 85 CT from 68 subjects with suspected encephalitis were rated independently by three neuroradiologists. They were blinded to patient and clinical details. The kappa value was good (0.65) for CT and moderate (0.59) for MRI. Agreement for HSV encephalitis was very good for CT (0.87) and MRI (0.82), but only fair for ADEM (0.32 CT; 0.31 MRI). Similarly, the overall sensitivity of imaging for HSV encephalitis was ~80% for both CT and MRI, whereas for ADEM, it was 0% for CT

and 20% for MRI. MRI specificity for HSV encephalitis between 3–10 days after symptom onset was 100%".

Sawlani V et al.[49] (2009) evaluated "45 confirmed cases of encephalitis (38 patients with JE and 7 patients with HSE) with MRI. CSF IgM MAC-ELISA and PCR were used for the diagnosis of JE and HSE, respectively. MRI findings were recorded in terms of site of involvement, the extent of lesions, visibility of each lesion on T2W, DWI and FLAIR sequences, and ADC calculations. They observed that in HSE, there was a significant restricted diffusion with low average ADC values observed in the acute stage and facilitated diffusion with high average ADC values observed in the chronic stage. Whereas JE lesions did not show restricted diffusion and significant low ADC values in the acute stage, though facilitated diffusion and high ADC values were observed in the chronic stage. They concluded that diffusion abnormality and conspicuity of lesions on DWI may be different in various acute encephalitis (HSE and JE). The ADC values are different in the acute stages of HSE and JE, reflecting the difference in the degree of diffusability of a water molecule. These observations may suggest that there may be an abundance of cytotoxic oedema in HSE and paucity of cytotoxic oedema in JE, in acute stage".

Misra UK et al.[50] (2008) evaluated "the prognostic role of MRI and single-photon emission computed tomography (SPECT) changes in viral encephalitis. From 1997-2006, 31 encephalitis subjects aged between 2-60 years were studied. The study population included 9 females and 22 males. Cranial MRI was done on a 1.5T scanner and 99mTc ethylene cysteine dimer (ECD) SPECT using a gamma camera. The outcome was defined at 6 months as complete, partial, or poor recovery. 19 patients had JE, one had HSE, and 11 had nonspecific encephalitis. Movement disorders were

present in 21, parkinsonian features in 19, and dystonia in 16 patients. MRI was abnormal in 20 patients and revealed thalamic involvement in 17, basal ganglia in eight, brainstem in 11, and cortical in two. SPECT revealed hypoperfusion in 22 patients, which was cortical in 11, thalamic in 10, basal ganglia in six, and midbrain in one. Cortical involvement was more frequently found by SPECT and brainstem involvement by MRI. The outcome of encephalitis did not differ in the different groups of encephalitis and MRI changes". They concluded that the spectrum of MRI findings did not correlate with the 6-month outcome.

Handique SK et al.[35] (2006) did neuroimaging on 62 JE patients with MRI or CT or both. MRI was done in 53 subjects. JE diagnosis was based on CSF IgM ELISA. "11 subjects (17.7%) showed temporal lobe involvement with abnormal MRI. All the patients showed hippocampal involvement. Two patients showed extension of lesions into the amygdala and uncus with insular involvement in 1. The rest of the temporal lobe was spared. All patients had thalamic and substantia nigra involvement with basal ganglia involvement in 7. They concluded that temporal lobe involvement pattern was fairly characteristic and involves the hippocampus, usually sparing the rest of the temporal lobe". They concluded that simultaneous involvement of basal ganglia, thalami, and substantia nigra helps in the differentiation of JE from HSE.

Misra UK et al.[33] (1994) evaluated 6 JE subjects. They observed that in MRI, there were brainstem abnormalities in three subjects and abnormalities of basal ganglia in one subject and spinal cord in one subject. They concluded that changes in MRI in the acute stage can provide early diagnostic clues for diagnosing and managing JE.

LACUNAE OF LITERATURE:

There is a lack of high-quality neuroimaging evidence for the evaluation of AES with various MRI sequences and their utility for day-to-day practice. The focus in the past has been only on the comparison of one or two MRI sequences against each other. The findings in MRI can be specific or non-specific, but they have a major role in the etiological diagnosis. There is a paucity of literature with regards to the yield of MRI and the role of various MRI sequences in subjects with clinical suspicion of AES.

MATERIAL AND METHODS:

Source of data:

Patients aged between 1 to 18 years presenting to "Department of Radio-Diagnosis at The KLE'S Dr. Prabhakar Kore Hospital & MRC, Belagavi."

Method of collection of data:

Study design: Hospital-based Cross-sectional study

Sample size: is calculated using the formula $4pq/d^2$, where p is the percentage of prevalence and q is (100-p), and d is the percentage likely difference in the prevalence (13%).

Here [3] p is 50%, by applying the formula, we get 4x50[100-50]/[13x13] = 60.

Sampling method: Universal sampling

Patients in the age group of 1 to 18 years were evaluated clinically and then undergo MRI performed using a 3.0 Tesla MRI scanner.

DURATION: One year – between 1st January 2020 to31st December 2020

INCLUSION CRITERIA: All patients in the age group of 1 year to 18 years with clinical features suggestive of acute encephalitis syndrome attended the department of radiodiagnosis in our hospital were included.

EXCLUSION CRITERIA: Patients with chromosomal genetic defects and congenital anomalies were excluded.

METHODOLOGY: Study was done using a 3.0 t MRI machine manufactured by siemens. Standard scan protocol was followed for all the patients undergoing mri.

Once the MRI was done, findings were noted and analyzed by a questionnaire which contains sociodemographic data, history taking, clinical examination, and MRI

scan findings. All the data collected was coded, entered in a Microsoft Excel sheet. Data analysis was done, and statistical tests were applied.

EQUIPMENT: 3.0T MRI manufactured by Siemens

MRI SEQUENCES THAT WERE OBTAINED:

- T1 weighted image.
- T2 weighted image.
- Diffusion-weighted imaging.
- Fluid attenuation inversion recovery.
- susceptibility-weighted imaging.
- Apparent diffusion co-efficient.
- Magnetic resonance spectroscopy.

STATISTICAL METHODS:

The study is of observational nature.

For the continuous quantitative variables, the mean and standard deviation were calculated.

Discrete variables were represented by a median. The categorical data were presented as rate, ratio, and proportion.

Suitable graphs will be used to depict the comparison. A p-value of less than 0.05 was the level for the results to be considered statistically significant.

For all the tests, the value of p less than 5% (0.05) was considered significant. Data was analyzed by using SPSS software, V.22.[51]

RESULTS:

The final analysis included a total of 68 participants.

Table 1: Descriptive analysis of age in the study population (N=68)

Age	Frequency	Percentage
1- 6 years	29	42.65%
6-12 years	18	26.47%
12-18 year	21	30.88%

Among the study population, the age group was 1- 6 years for 29 (42.65%) participants, 6- 12 years for 18 (26.47%) participants, and 12-18 years for 21 (30.88%) participants. (Table 1 & Figure 13)

Figure 13: Bar chart for age group (N=68)

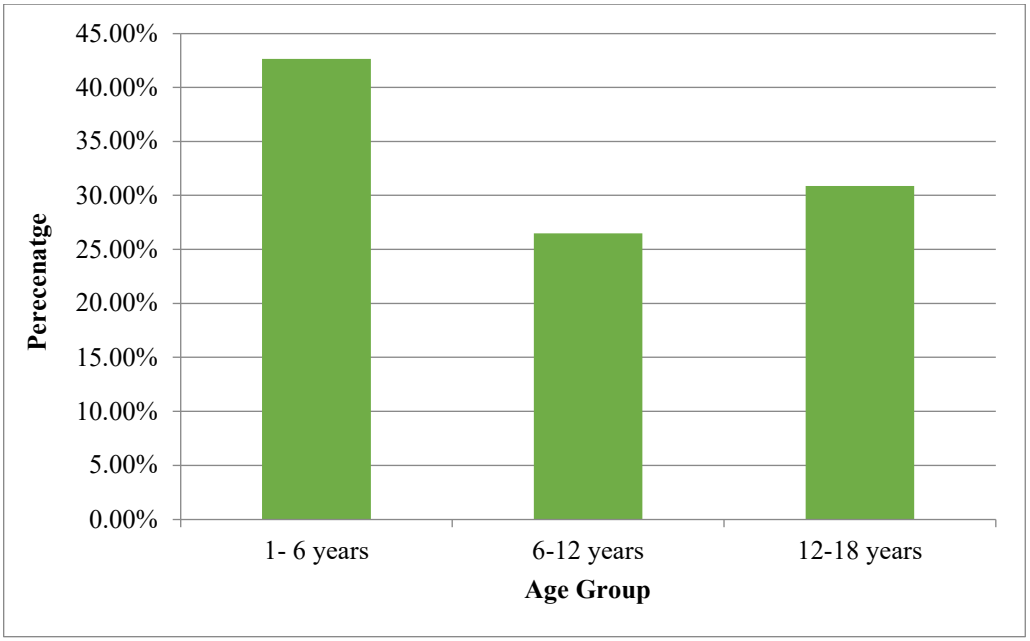


Table 2: Descriptive analysis of sex in the study population (N=68)

Sex	Frequency	Percentages
Female	25	36.76%
Male	43	63.24%

Among the study population, there were 25 (36.76%) female participants and 43 (63.24%) male participants. (Table 2 & Figure 14)

Figure 14: Pie chart for gender (N=68)

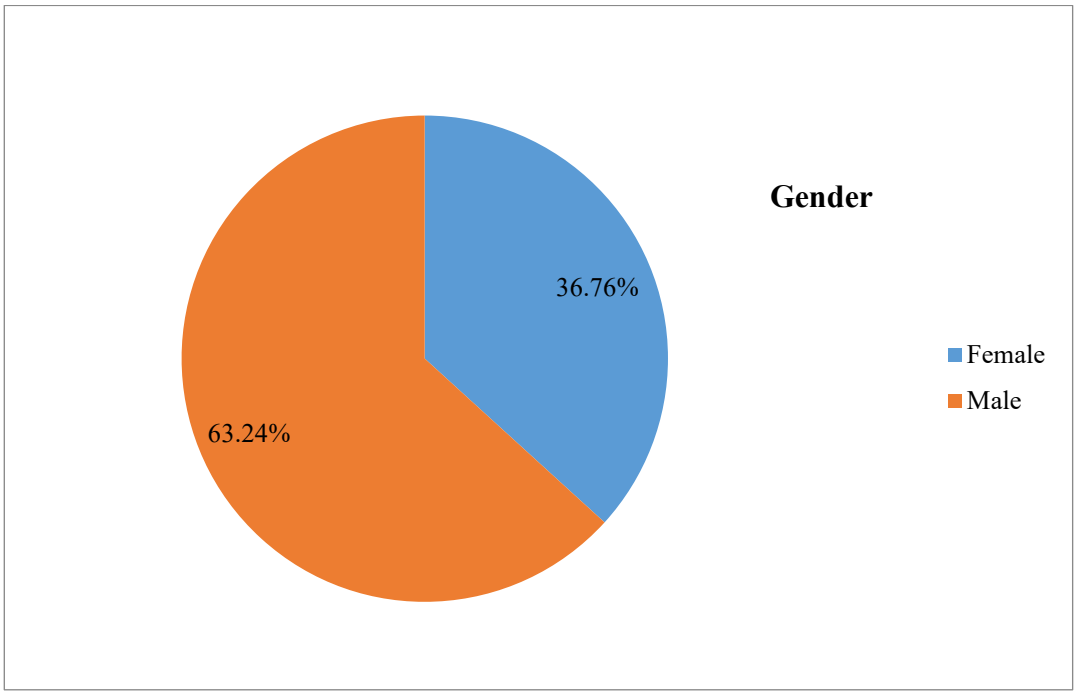


Table 3: Descriptive analysis of birth history in the study population (N=68)

Birth History	Frequency	Percentages
Normal	53	77.94%
NICU Admission	15	22.06%

Among the study population, the birth history was normal for 53 (77.94%) participants and NICU admission for 15 (22.06%) participants. (Table 3 & Figure 15)

Figure 15: Pie chart for birth history (N=68)

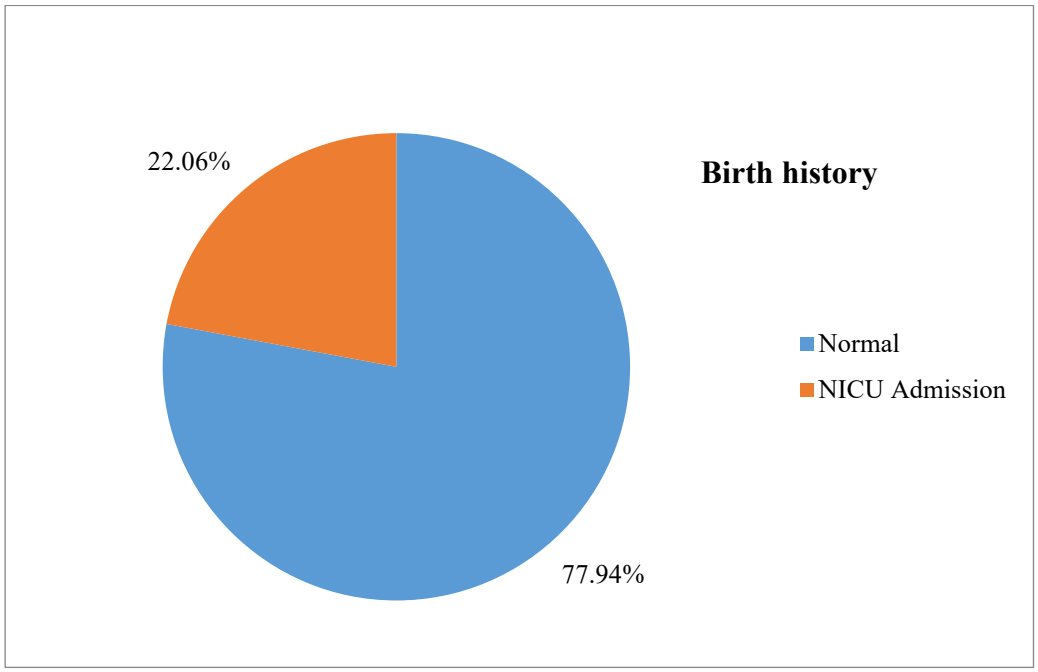


Table 4: Descriptive analysis of developmental history in the study population (N=68)

Developmental History	Frequency	Percentages
Normal	67	98.53%
Head circumference below 3rd centile	1	1.47%

Among the study population, the developmental history was normal for 67 (98.53%) participants and abnormal (head circumference below 3rd centile) for 1 (1.47%) participant.

Table 5: Descriptive analysis of immunization history in the study population (N=68)

Immunization History	Frequency	Percentages
Up to date	56	82.35%
Not up to date	12	17.65%

Among the study population, the immunization history was up to date for 56 (82.35%) participants and not up to date for 12 (17.65%) participants. (Table 5)

Table 6: Descriptive analysis of past history in the study population (N=68)

Past History	Frequency	Percentages
History of recurrent respiratory tract infections	16	23.53%
History of recurrent gastroenteritis	5	7.35%
Past history of dengue fever	3	4.41%
Nothing significant	44	64.71%

Among the study population, the past history present was a history of recurrent respiratory tract infections for 16 (23.53%) participants, a history of recurrent gastroenteritis for 5 (7.35%) participants, and past history of dengue fever for 3 (4.41%) participants. (Table 6 & Figure 16)

Figure 16: Bar chart for past history (N=68)

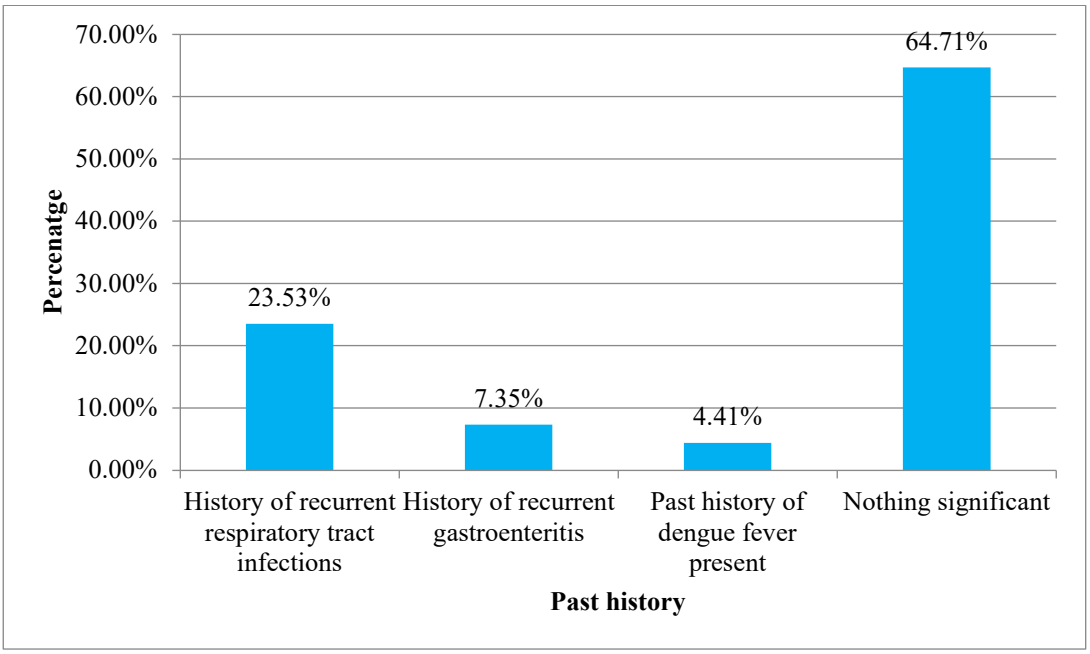


Table 7: Descriptive analysis of past history in the study population where MRI was suggestive of AES (N=42)

Past History	Frequency	Percentages
History of recurrent respiratory tract infections (N=11)		
Infectious	4	36.36%
Non-infectious	2	18.18%
Para infectious	5	45.46%
History of recurrent gastroenteritis (N=5)		
Infectious	0	0%
Non-infectious	1	20%
Para infectious	4	80%
Past history of dengue fever present (N=3)		
Infectious	0	0%
Non-infectious	0	0%
Para infectious	3	100%
Nothing significant	23	54.76%

Among the study population where MRI radiological findings were suggestive of AES, the past history was a history of recurrent respiratory tract infections for 11 (26.19%) participants (36.36% infectious, 18.18% non-infectious, and 45.46% para-infectious), history of recurrent gastroenteritis for 5 (11.90%) participants (0% infectious, 80% non-infectious and 20% para-infectious), past history of dengue fever

present for 3 (7.14%) participants (0% infectious, 0% non-infectious and 100% para-infectious) and nothing significant for 23 (54.76%) participants. (Table 7 & Figure 17)

Figure 17: Clustered bar chart of past history for MRI radiological findings suggestive of AES (N=42)

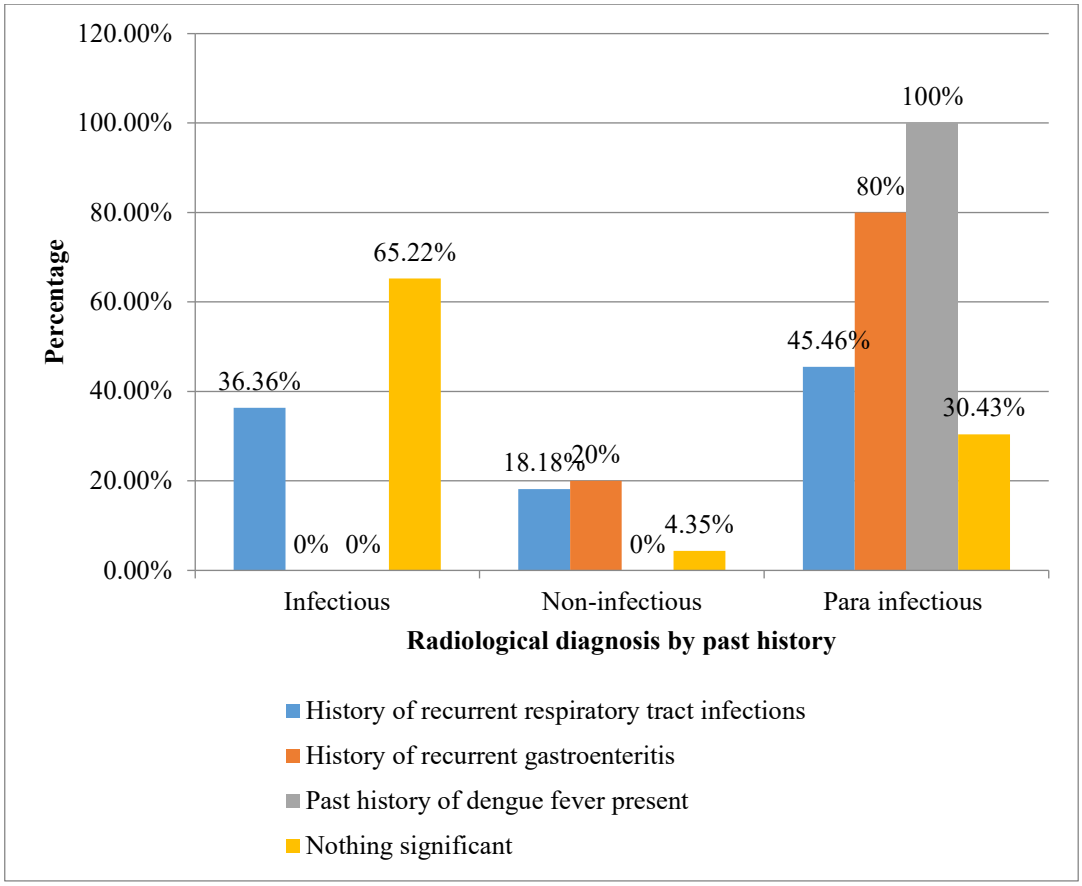


Table 8: Descriptive analysis of symptoms where MRI showed features of acute encephalitis syndrome (N=42)

Symptoms	Frequency	Percentage
Fever	33	78.57%
Convulsions	19	45.24%
Limb stiffness/ weakness	18	42.86%
Altered sensorium	3	7.14%
Headache	3	7.14%
Vomiting	3	7.14%
Delusion	3	7.14%
Seizures	2	4.76%
Depressive behavior	2	4.76%
Blurred vision	1	2.38%
Decreased awareness	1	2.38%
Aggressive behavior	1	2.38%
Drowsiness	1	2.38%

Among the study population, the major symptoms were fever in 33 (78.57%) participants, convulsions in 19 (45.24%) participants, limb stiffness/weakness in 18 (42.86%) participants, altered sensorium, headache, vomiting, and seizures in 3 (7.14%) participants. (Table 8 & Figure 18)

Figure 18: Bar chart for symptoms for MRI radiological findings suggestive of AES (N=42)

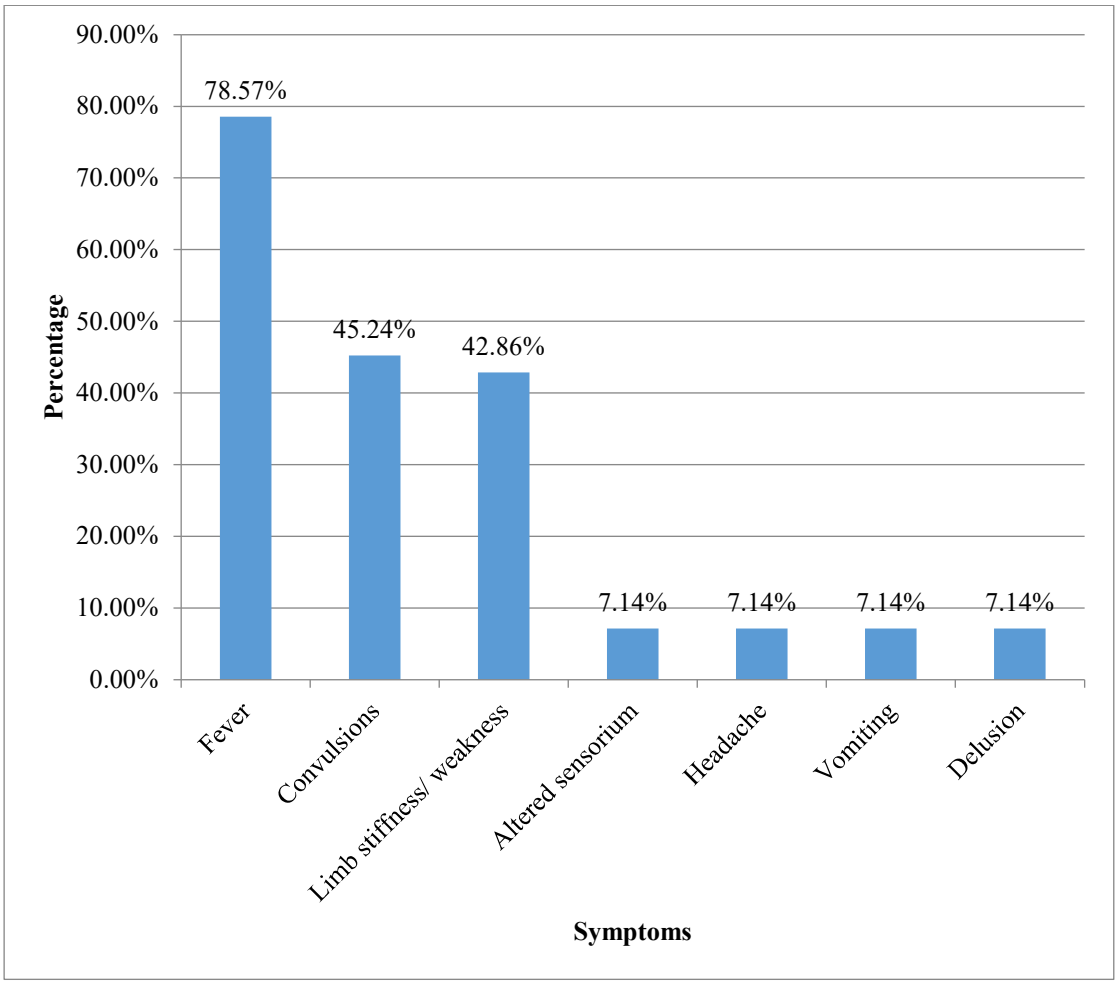


Table 9: Descriptive analysis of MRI yield for AES in the study population (N=68)

MRI Yield	Frequency	Percentages
MRI Positive for AES	42	61.76%
MRI Negative for AES	26	38.24%

Among the study population, the MRI yield was MRI Positive for AES for 42 (61.76%) participants and MRI Negative for AES for 26 (38.24%) participants. (Table 9 & Figure 19)

Figure 19: Pie chart for MRI yield (N=68)

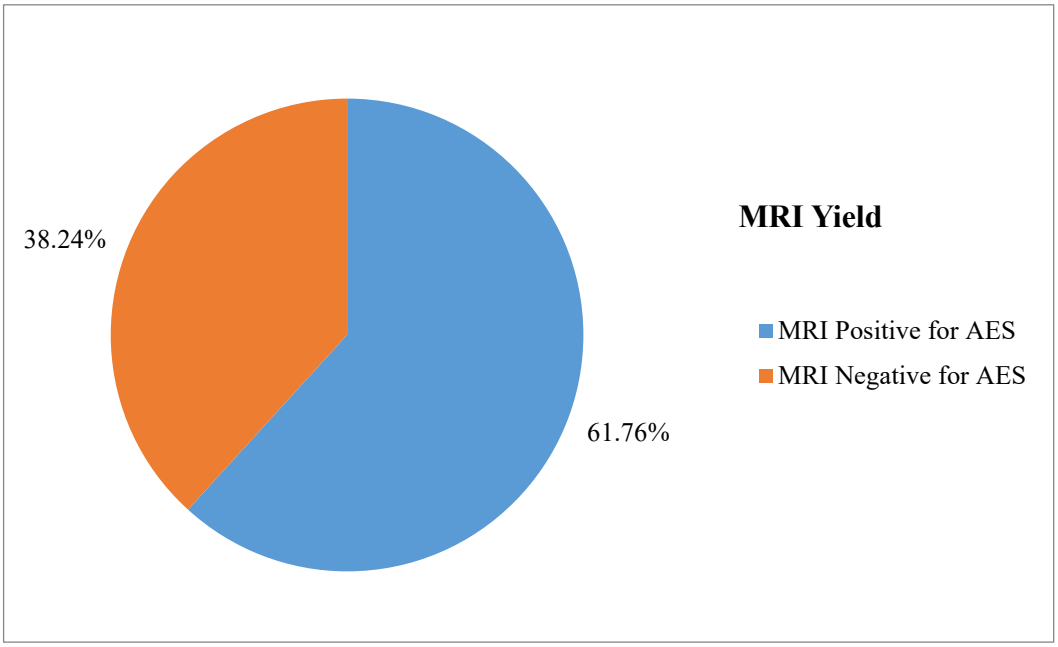


Table 10: Descriptive analysis of MRI anatomical location suspected to have AES in the study population (N=68)

Anatomical location	Normal		MRI suggestive of AES	
	Frequency	Percentages	Frequency	Percentages
Frontal lobe	40	58.80%	28	41.20%
Parietal lobe	41	60.30%	27	39.70%
Temporal lobe	39	57.40%	29	42.60%
Occipital lobe	56	82.40%	12	17.60%
Centrum Semiovale	57	83.80%	11	16.20%
Corona Radiata	62	91.20%	6	8.80%
Corpus Callosum	62	91.20%	6	8.80%
Caudate Nucleus	59	86.80%	9	13.20%
Lentiform Nucleus	54	79.40%	14	20.60%
Subthalamic Nucleus	68	100%	0	0%
Substantia Nigra	68	100%	0	0%
Cerebellar hemisphere	61	89.70%	7	10.30%
Median Vermis	66	97.10%	2	2.90%
Thalamus	54	79.40%	14	20.60%
Tectum	67	98.50%	1	1.50%
Tegmentum	65	95.60%	3	4.40%

Cerebral Peduncles	66	97.10%	2	2.90%
Corpora Quadrigemia	68	100%	0	0%
Posterior perforated substance	68	100%	0	0%
Periaqueductal grey	68	100%	0	0%
Internal capsule	65	95.60%	3	4.40%
Cerebellar Peduncles	65	95.60%	3	4.40%
Pons	62	91.20%	6	8.80%
Medulla oblongata	65	95.60%	3	4.40%

Among the study population for normal MRI yield, the anatomical location was frontal lobe for 40 (58.8%) participants, parietal lobe for 41 (60.3%) participants, temporal lobe for 39 (57.4%) participants, occipital lobe for 56 (82.4%) participants, Centrum Semiovale for 57 (83.8%) participants, Corona Radiata for 62 (91.2%) participants, Corpus Callosum for 62 (91.2%) participants, Caudate Nucleus for 59 (86.8%) participants, Lentiform Nucleus for 54 (79.4%) participants, Subthalamic Nucleus for 68 (100%) participants, Substantia Nigra for 68 (100%) participants, Cerebellar hemisphere for 61 (89.7%) participants, Median Vermis for 66 (97.1%) participants, Thalamus for 54 (79.4%) participants, Tectum for 67 (98.5%) participants, Tegmentum for 65 (95.6%) participants, Cerebral Peduncles for 66 (97.1%) participants, Corpora Quadrigemia, Posterior perforated substance, Periaqueductal grey for 68 (100%) participants, Internal capsule, Medulla oblongata for 65 (95.6%) participants, and pons for 62 (91.2%) participants. Among the study

population for MRI yield suggestive of AES, the anatomical location was frontal lobe for 28 (41.2%) participants, the parietal lobe for 27 (39.7%) participants, temporal lobe for 29 (42.6%) participants, occipital lobe for 12 (17.6%) participants, Centrum Semiovale for 11 (16.2%) participants, Corona Radiata for 6 (8.8%) participants, Corpus Callosum for 6 (8.8%) participants, Caudate Nucleus for 9 (13.2%) participants, Lentiform Nucleus for 14 (20.6%) participants, Subthalamic Nucleus for no participant, Substantia Nigra for no participant, Cerebellar hemisphere for 7 (10.3%) participants, Median Vermis for 2 (2.9%) participants, Thalamus for 14 (20.6%) participants, Tectum for 1 (1.5%) participants, Tegmentum for 3 (4.4%) participants, Cerebral Peduncles for 2 (2.9%) participants, Corpora Quadrigemia, Posterior perforated substance, Periaqueductal grey for no participant, Internal capsule, Medulla oblongata for 3 (4.4%) participants, and pons for 6 (8.8%) participants. (Table 10)

Table 11: Descriptive analysis of MRI radiological findings suggestive of AES in the study population (N=42)

N=17: Normal study

Radiological diagnosis	Frequency	Percentages
Infectious	19	45.24%
Non-infectious	4	9.52%
Para infectious	19	45.24%

Among the study population where MRI radiological findings were suggestive of AES, the radiological diagnosis was infectious for 19 (45.24%) participants, non-infectious for 4 (9.52%) participants, and para infectious for 19 (45.24%) participants. (Table 11 & Figure 20)

Figure 20: Bar chart for radiological diagnosis suggestive of AES (N=42)

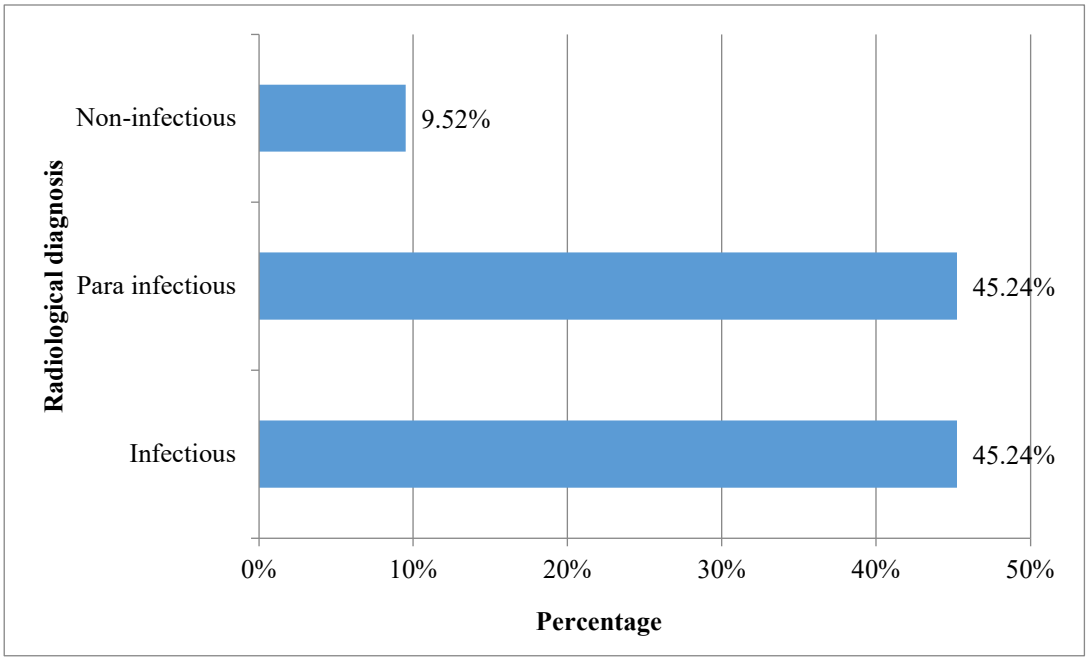


Table 12: Descriptive analysis of MRI radiological findings in study population which were suspected to be AES but are not AES (N=9)

Radiological diagnosis	Frequency	Percentages
Pansinusitis	3	33.33%
Acute leukoencephalopathy with restricted diffusion	1	11.11%
Arachnoid cyst in the left anterior temporal lobe	1	11.11%
Left mesial temporal sclerosis	1	11.11%
Periventricular and subcortical leukomalacia	1	11.11%
Posterior reversible encephalopathy syndrome	1	11.11%
Sequelae changes to neonatal hypoximc ischemic injury	1	11.11%

Among the study population, MRI radiological findings were not suggestive of AES for 9 (13.23%) participants. The radiological diagnosis in such cases was Pansinusitis for 3 (33.33%) participants, Acute leukoencephalopathy with restricted diffusion, Arachnoid cyst in the left anterior temporal lobe, Left mesial temporal sclerosis, Periventricular and subcortical leukomalacia, Posterior reversible encephalopathy syndrome, and Sequlae changes to neonatal hypoximc ischemic injury for 1 (11.11%) participants each. (Table 12)

Table 13: Descriptive analysis of most common involved anatomical locations where MRI showed features of acute encephalitis syndrome (N=68)

Anatomical location	MRI suggestive of AES	
	Frequency	Percentages
Frontal lobe	29	69.05%
Parietal lobe	27	64.28%
Temporal lobe	28	66.67%
Lentiform Nucleus	14	33.33%
Thalamus	14	33.33%
Occipital lobe	12	28.57%
Centrum Semiovale	11	26.19%
Caudate Nucleus	9	21.43%
Cerebellar hemisphere	7	16.67%
Corona Radiata	6	14.28%
Corpus Callosum	6	14.28%
Pons	6	14.28%
Tegmentum	3	7.14%
Internal capsule	3	7.14%
Cerebellar Peduncles	3	7.14%
Medulla oblongata	3	7.14%

Cerebral Peduncles	2	4.76%
Median Vermis	2	4.76%
Tectum	1	2.38%
Subthalamic Nucleus	0	0%
Substantia Nigra	0	0%
Corpora Quadrigemia	0	0%
Posterior perforated substance	0	0%
Periaqueductal grey	0	0%

Among the study population for MRI yield suggestive of AES, the anatomical location was frontal lobe for 29 (69.05%) participants, parietal lobe for 27 (64.28%) participants, temporal lobe for 28 (66.67%) participants, occipital lobe for 12 (28.57%) participants, Centrum Semiovale for 11 (26.19%) participants, Corona Radiata for 6 (14.28%) participants, Corpus Callosum for 6 (14.28%) participants, Caudate Nucleus for 9 (21.43%) participants, Lentiform Nucleus for 14 (33.33%) participants, Subthalamic Nucleus for no participant, Substantia Nigra for no participant, Cerebellar hemisphere for 7 (16.67%) participants, Median Vermis for 2 (4.76%) participants, Thalamus for 14 (33.33%) participants, Tectum for 1 (2.38%) participants, Tegmentum for 3 (7.14%) participants, Cerebral Peduncles for 2 (4.76%) participants, Corpora Quadrigemia, Posterior perforated substance, Periaqueductal grey for no participant, Internal capsule, Medulla oblongata for 3 (7.14%) participants, and pons for 6 (14.28%) participants. (Table 13)

Table 14: Descriptive analysis of basic MRI sequences to yield clues to diagnose non-infectious acute encephalitis syndrome by radiological diagnosis (N=4)

Basic MRI sequences	Frequency	Percentages
T1	3	75.00%
T2	4	100.00%

Among the study population, the basic MRI sequence to yield clues to diagnose non-infectious AES was T1 for 3 (75%) participants and T2 for 4 (100%) participants. (Table 14)

Table 15: Descriptive analysis of basic MRI sequences to yield clues to diagnose infectious acute encephalitis syndrome by radiological diagnosis (N=19)

Basic MRI sequences	Frequency	Percentages
T1	4	21.05%
T2	17	89.47%

Among the study population, the basic MRI sequence to yield clues to diagnose infectious AES was T1 for 4 (21.05%) participants and T2 for 17 89.47%) participants. (Table 15).

Table 16: Descriptive analysis of basic MRI sequences to yield clues to diagnose para-infectious acute encephalitis syndrome by radiological diagnosis (N=19)

Basic MRI sequences	Frequency	Percentages
T1	12	63.16%
T2	19	100.00%

Among the study population, the basic MRI sequence to yield clues to diagnose para infectious AES was T1 for 12 (63.16%) participants and T2 for 19 (100%) participants. (Table 16)

Table 17: Descriptive analysis of special MRI sequences to yield clues to diagnose non- infectious acute encephalitis syndrome by radiological diagnosis (N=4)

Special MRI sequences	Frequency	Percentages
FLAIR	4	100.00%
DWI	3	75.00%
SWI	0	0.00%
ADC	3	75.00%
MRS	0	0.00%

Among the study population, the special MRI sequence to yield clues to diagnose non-infectious AES was FLAIR for 4 (100%) participants, DWI for 3 (75%) participants, SWI and MRS for no participant, and ADC for 3 (75%) participants. (Table 17 & Figure 21).

Figure 21: Bar chart for special MRI sequence to yield clues to diagnose non-infectious AES (N=4)

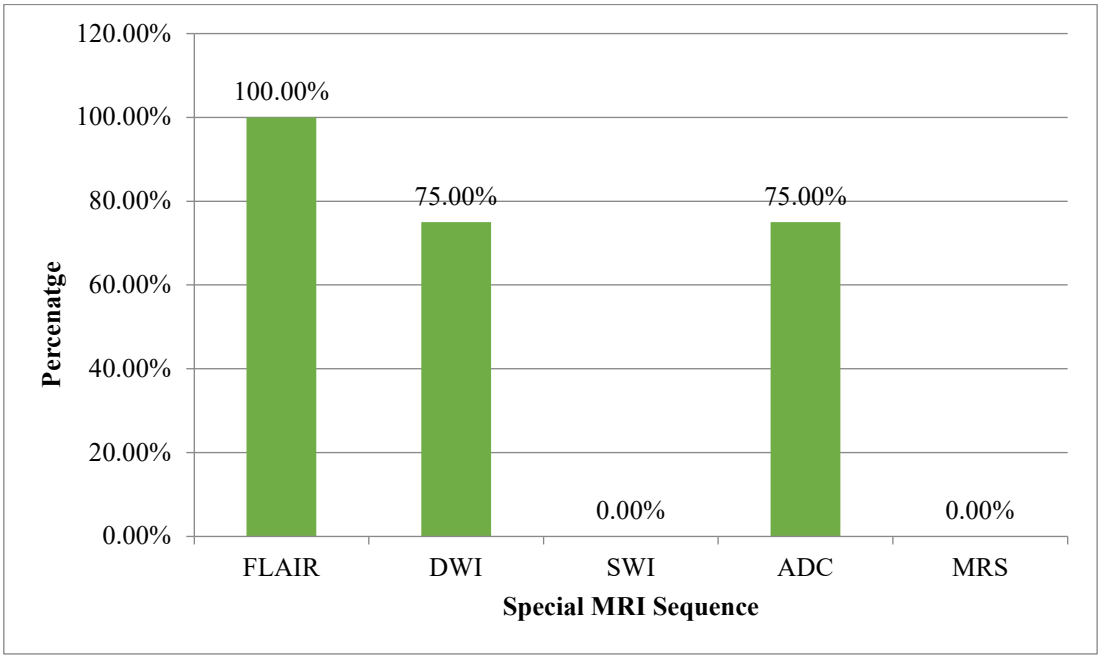


Table 18: Descriptive analysis of special MRI sequences to yield clues to diagnose infectious acute encephalitis syndrome by radiological diagnosis (N=19)

Special MRI sequences	Frequency	Percentages
FLAIR	13	68.42%
DWI	6	31.58%
SWI	0	0.00%
ADC	7	36.84%
MRS	0	0.00%

Among the study population, the special MRI sequence to yield clues to diagnose infectious AES was FLAIR for 13 (68.42%) participants, DWI for 6 (31.58%) participants, SWI and MRS for no participant, and ADC for 7 (36.84%) participants. (Table 18 & Figure 22)

Figure 22: Bar chart for special MRI sequence to yield clues to diagnose infectious AES (N=19)

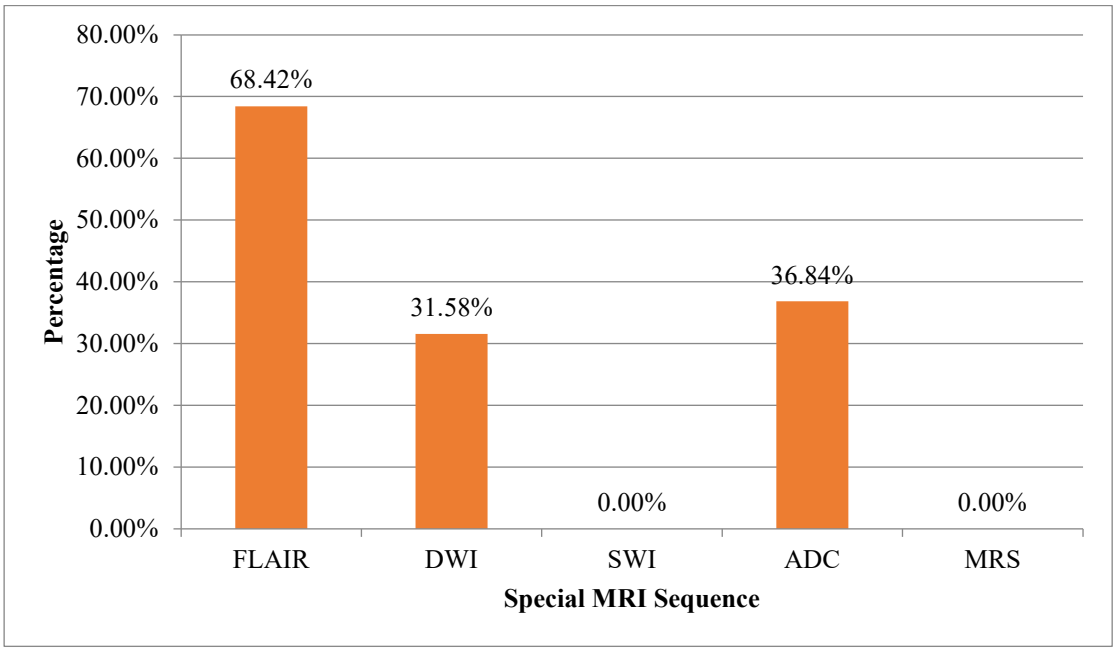


Table 19: Descriptive analysis of special MRI sequences to yield clues to diagnose para infectious acute encephalitis syndrome by radiological diagnosis (N=19)

Special MRI sequences	Frequency	Percentages
FLAIR	19	100.00%
DWI	11	57.89%
SWI	9	47.37%
ADC	11	57.89%
MRS	1	5.26%

Among the study population, the special MRI sequence to yield clues to diagnose infectious AES was FLAIR for 19 (100%) participants, DWI for 11 (57.89%) participants, SWI for 9 (47.37%) participants, MRS for 1 (5.26%) participant and ADC for 11 (57.89%) participants. (Table 19 & Figure 23)

Figure 23: Bar chart for special MRI sequence to yield clues to diagnose para infectious AES (N=19)

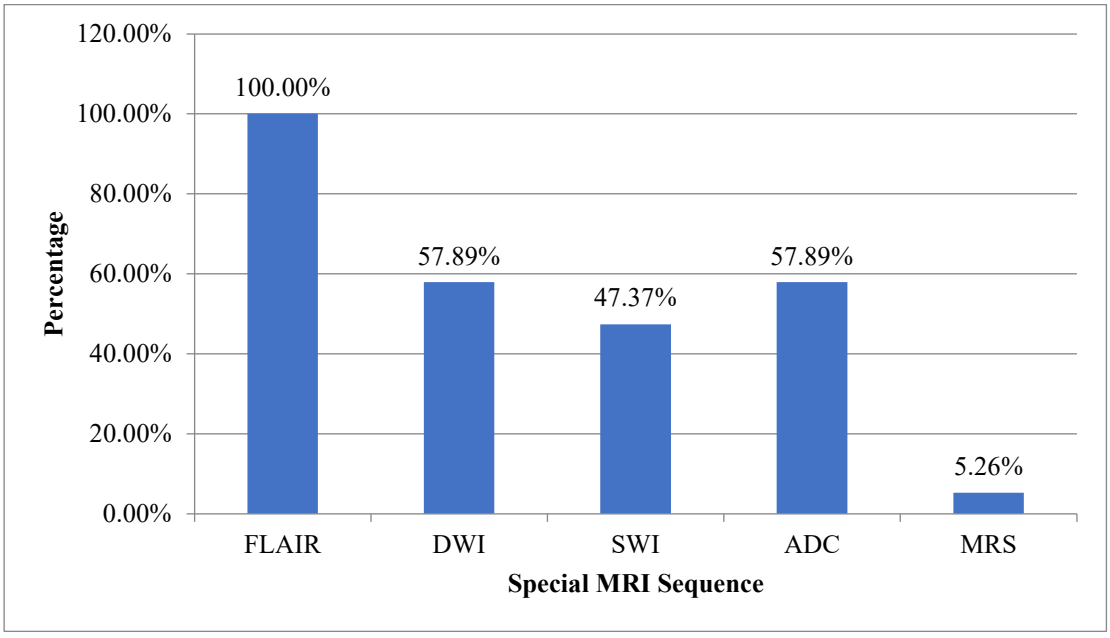


Table 20: Descriptive analysis of MRI radiological findings suggestive of AES by age in the study population (N=42)

Radiological diagnosis by age	Frequency	Percentage
1-6 years (N=19)		
Non-infectious	1	5.26%
Para infectious	11	57.89%
Infectious	7	36.84%
6 - 12 years (N=10)		
Non-infectious	1	10%
Para infectious	2	20%
Infectious	7	70%
12-18 years (N=13)		
Non-infectious	2	15.38%
Para infectious	6	46.15%
Infectious	5	38.46%

Out of 19 participants for which MRI radiological findings were suggestive of AES in age group 1-6 years, the radiological diagnosis was infectious for 7 (36.84%) participants, non-infectious for 1 (5.26%) participants, and para infectious for 11 (57.89%) participants. Out of 10 participants for which MRI radiological findings were suggestive of AES in age group 6-12 years, the radiological diagnosis was infectious for 7 (70%) participants, non-infectious for 1 (10%) participants, and para

infectious for 2 (20%) participants. Out of 13 participants for which MRI radiological findings were suggestive of AES in the age group 12 - 18 years, the radiological diagnosis was infectious for 5 (38.46%) participants, non-infectious for 2 (15.38%) participants, and para infectious for 6 (46.15%) participants. (Table 20 & Figure 24).

Figure 24: Clustered bar chart for MRI radiological findings suggestive of AES by age (N=42)

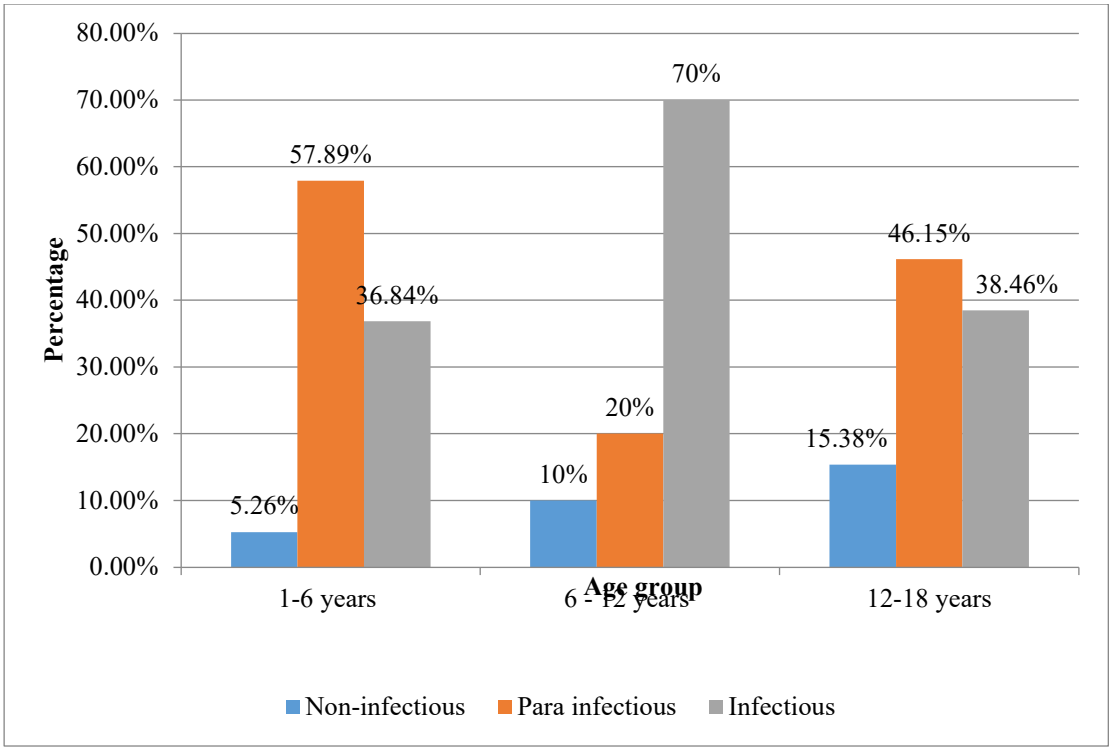


Table 21: Descriptive analysis of MRI radiological findings suggestive of AES by gender in the study population (N=42)

Radiological diagnosis by gender	Frequency	Percentages
Female MRI suggestive of AES (N=18)		
Non-infectious	1	5.56%
Para infectious	9	50.00%
Infectious	8	44.44%
Male MRI suggestive of AES (N=24)		
Non-infectious	3	12.50%
Para infectious	10	41.67%
Infectious	11	45.83%

Out of 18 female participants for which MRI radiological findings were suggestive of AES, the radiological diagnosis was infectious for 8 (44.44%) participants, non-infectious for 1 (5.56%) participants, and para infectious for 9 (50.00%) participants. Out of 24 male participants for which MRI radiological findings were suggestive of AES, the radiological diagnosis was infectious for 11 (45.83%) participants, non-infectious for 3 (12.50%) participants, and para infectious for 10 (41.67%) participants. (Table 21 & Figure 25).

Figure 25: Bar chart for MRI radiological findings suggestive of AES by gender (N=42)

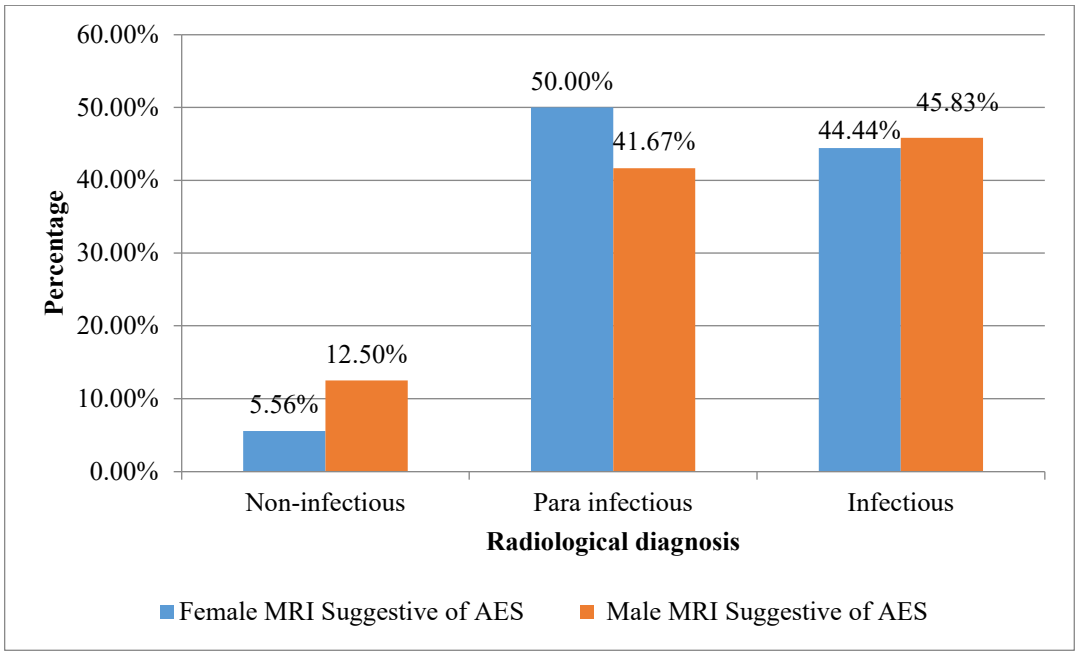


Table 22: Descriptive analysis of anti-MOG antibody results in cases where MRI was suggestive of ADEM/autoimmune encephalitis (N=9)

Anti MOG antibody	MRI suggestive of ADEM	MRI suggestive of autoimmune encephalitis
Positive (N=1)	1 (100%)	0 (0%)
Negative (N=9)	6 (66.67%)	3 (33.33%)

Out of 1 participant with a positive anti-MOG antibody, the MRI radiological findings were suggestive of ADEM for 1 (100%) participant and autoimmune encephalitis for no participant. Out of 9 participants with negative anti-MOG antibody, the MRI radiological findings were suggestive of ADEM for 6 (66.67%) participants and autoimmune encephalitis for 3 (33.33%) participants. (Table 22)

Table 23: Descriptive analysis of EEG laboratory findings in cases where MRI radiological findings were suggestive of AES (N=42)

EEG laboratory findings	Frequency	Percentages
Normal	16	38.10%
Abnormal	26	61.90%

Among the study population where MRI radiological findings were suggestive of AES, the EEG laboratory findings were normal for 16 (38.1%) participants and abnormal for 26 (61.9%) participants. (Table 23 & Figure 23)

Figure 26: Pie chart for EEG laboratory findings (N=42)

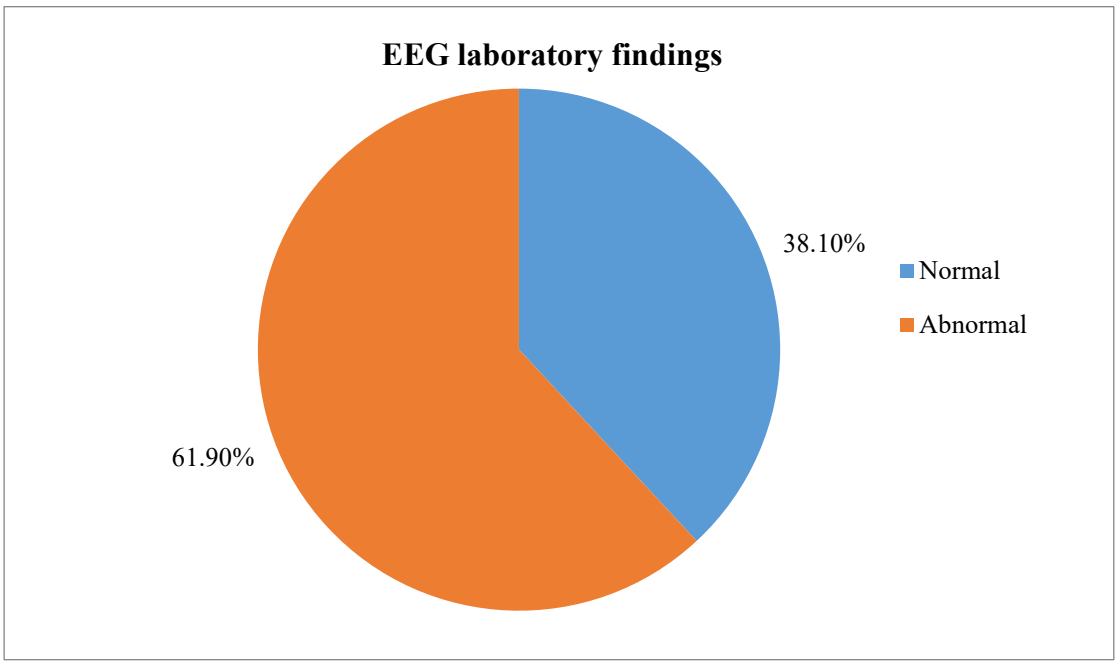


Table 24: Descriptive analysis of EEG laboratory findings in cases where MRI radiological findings suggestive of infectious AES (N=19)

EEG laboratory findings	Frequency	Percentages
Normal	10	52.60%
Abnormal	9	47.40%

Out of 19 participants for whom MRI radiological findings were suggestive of infectious AES, the EEG laboratory findings were normal for 10 (52.6%) participants and abnormal for 9 (47.4%) participants. (Table 24)

Table 25: Descriptive analysis of EEG laboratory findings in cases where MRI radiological findings suggestive of non-infectious AES (N=4)

EEG laboratory findings	Frequency	Percentages
Normal	1	25%
Abnormal	3	75%

Out of 4 participants for whom MRI radiological findings were suggestive of non-infectious AES, the EEG laboratory findings were normal for 1 (25%) participant and abnormal for 3 (75%) participants. (Table 25)

Table 26: Descriptive analysis of EEG laboratory findings in cases where MRI radiological findings suggestive of para infectious AES (N=19)

EEG laboratory findings	Frequency	Percentages
Normal	5	26.30%
Abnormal	14	73.70%

Out of 19 participants for whom MRI radiological findings were suggestive of para-infectious AES, the EEG laboratory findings were normal for 5 (26.3%) participants and abnormal for 14 (73.7%) participants. (Table 26)

Table 27: Descriptive analysis of status epilepticus in cases where MRI was suggestive of AES (N=42)

Status Epilepticus	Frequency	Percentages
Present	5	11.90%
Non-infectious	0	0%
Para infectious	5	100%
Infectious	0	0%
Absent	37	88.10%

Among the study population where MRI radiological findings were suggestive of AES, the status epilepticus was present for 5 (11.90%) participants and absent for 37 (88.10%) participants. Out of 5 participants with status epilepticus present, the radiological diagnosis was infectious for no participant, non-infectious for no participant, and para infectious for 5 (100%) participants. (Table 27 & Figure 27)

Figure 27: Bar chart for status epilepticus (N=42)

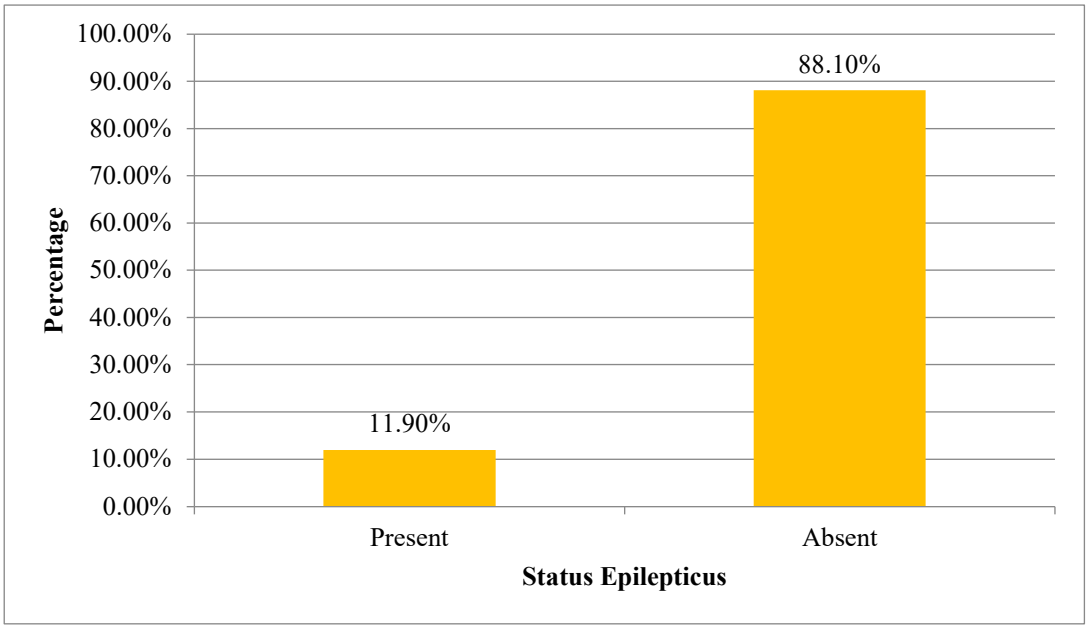


Table 28: Descriptive analysis of CSF report in cases where MRI was suggestive of AES (N=42)

CSF Report	Frequency	Percentages
Normal	20	47.62%
Non-infectious	2	10%
Para infectious	8	40%
Infectious	10	50%
Abnormal	22	52.38%
Non-infectious	2	9.09%
Para infectious	11	50.00%
Infectious	9	40.91%

Among the study population where MRI radiological findings were suggestive of AES, the CSF report was normal for 20 (47.62%) participants and abnormal for 22 (52.38%) participants. Out of 20 participants for with normal CSF report, the radiological diagnosis was infectious for 10 (50%) participants, non-infectious for 2 (10%) participants, and para infectious for 8 (40%) participants. Out of 22 participants for with abnormal CSF report, the radiological diagnosis was infectious for 9 (40.91%) participants, non-infectious for 2 (9.09%) participants, and para infectious for 11 (50%) participants. (Table 28 & Figure 28, 29)

Figure 28: Bar chart for CSF report (N=42)

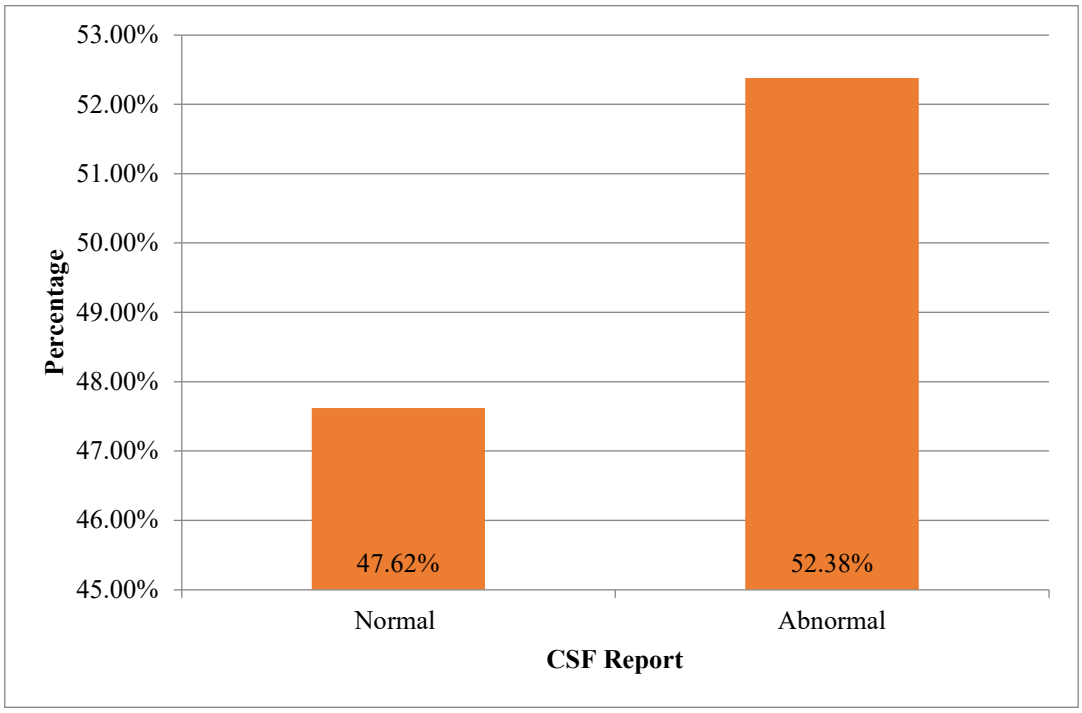


Figure 29: Clustered bar chart CSF report where MRI was suggestive of AES (N=42)

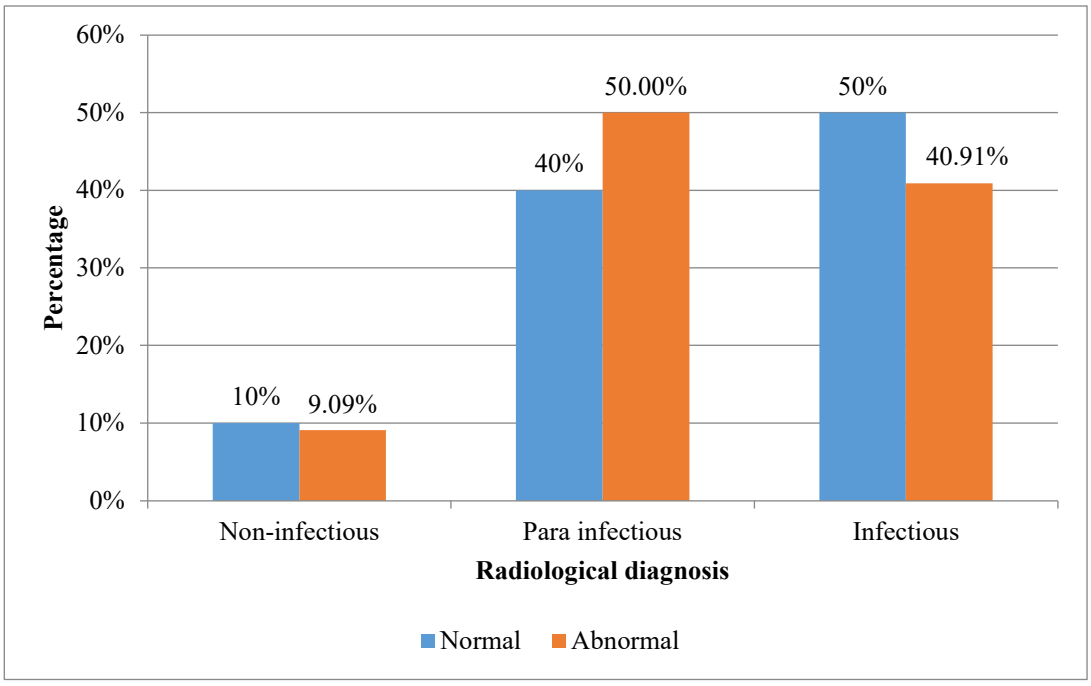


Table 29: Descriptive analysis of basic MRI sequences (T1 & T2) where MRI was suggestive of AES (N=42)

Basic MRI Sequence	T1		T2	
	Frequency	**Percentages**	**Frequency**	**Percentages**
Infectious (N=19)				
Isointense	15	78.95%	2	10.53%
Hypointense	4	21.05%	0	0.00%
Hyperintense	0	0.00%	17	89.47%
Para infectious (N=19)				
Isointense	7	36.84%	0	0.00%
Hypointense	12	63.16%	0	0.00%
Hyperintense	0	0.00%	19	100%
Non-infectious (N=4)				
Isointense	1	25.00%	0	0.00%
Hypointense	3	75.00%	0	0.00%
Hyperintense	0	0.00%	4	100%

Out of 19 participants for whom MRI radiological findings were suggestive of infectious AES, the **basic MRI sequence - T1** was isointense for 15 (78.95%) participants, Hypointense for 4 (21.05%) participants, and Hyperintense for no participant. Out of 19 participants for whom MRI radiological findings were suggestive of para-infectious AES, the basic MRI sequence - T1 was isointense for 7

(36.84%) participants, Hypointense for 12 (63.16%) participants, and Hyperintense for no participant. Out of 4 participants for whom MRI radiological findings were suggestive of non-infectious AES, the basic MRI sequence - T1 was isointense for 1 (25%) participants, Hypointense for 3 (75%) participants, and Hyperintense for no participant.

Out of 19 participants for whom MRI radiological findings were suggestive of infectious AES, the **basic MRI sequence – T2** was isointense for 2 (10.53%) participants, Hypointense for no participant, and Hyperintense for 17 (89.47%) participants. Out of 19 participants for whom MRI radiological findings were suggestive of para-infectious AES, the **basic MRI sequence – T2** was isointense for no participant, Hypointense for no participant, and Hyperintense for 19 (100%) participants. Out of 4 participants for whom MRI radiological findings were suggestive of non-infectious AES, the **basic MRI sequence – T2** was isointense for no participant, Hypointense for no participant, and Hyperintense for 4 (100%) participants. (Table 29 & Figure 30, 31)

Figure 30: Clustered bar chart basic MRI sequence – T1 where MRI was suggestive of AES (N=42)

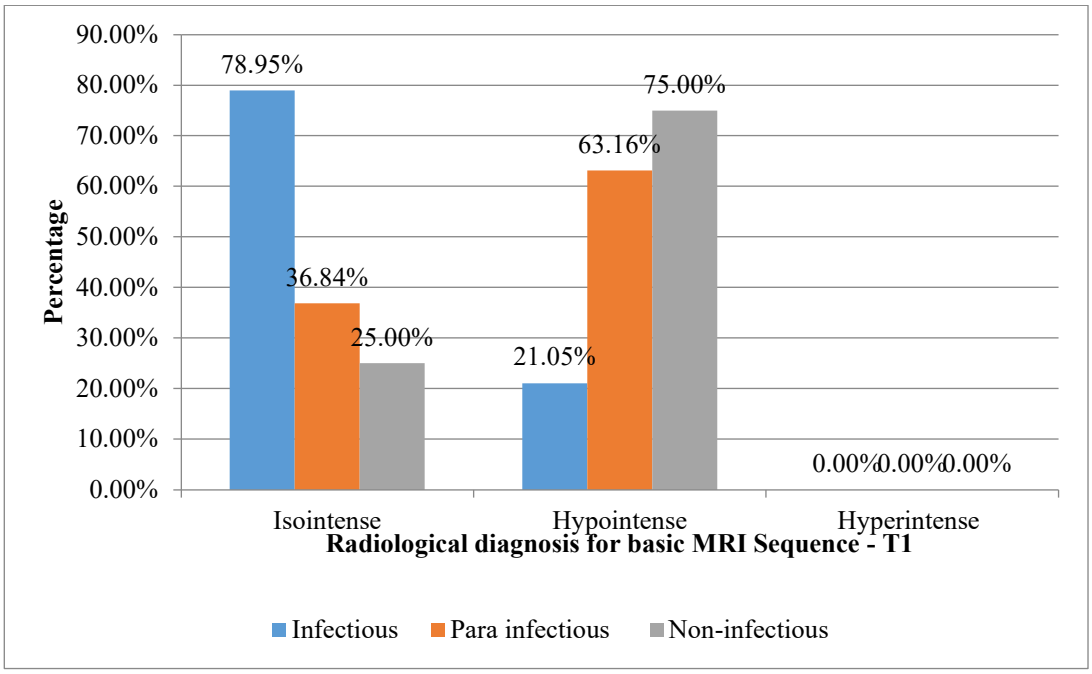


Figure 31: Clustered bar chart basic MRI sequence – T2 where MRI was suggestive of AES (N=42)

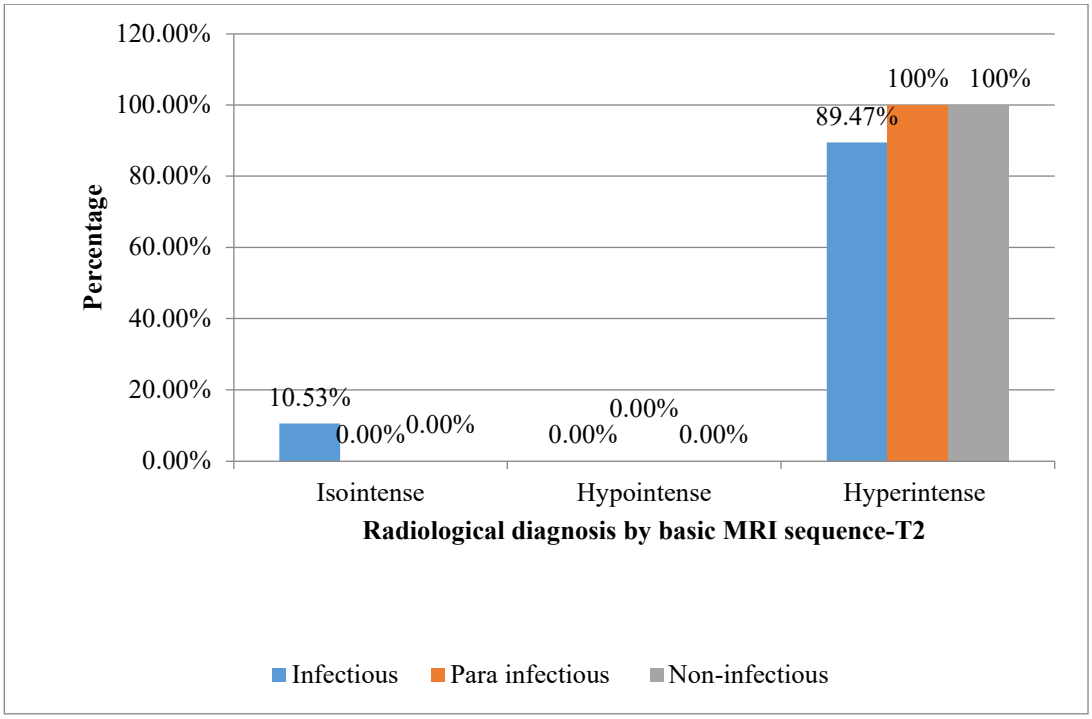


Table 30: Descriptive analysis of special MRI sequences (FLAIR), which shows signal intensity changes where MRI was suggestive of AES (N=42)

Signal intensity	Frequency	Percentages
Isointense	6	14.29%
Infectious	6	100%
Non-infectious	0	0%
Para infectious	0	0%
Hypointense	0	0%
Hyperintense	36	85.71%
Infectious	13	36.11%
Non-infectious	4	11.11%
Para infectious	19	52.78%

Among the study population where MRI radiological findings were suggestive of AES, the signal intensity for special MRI sequence - FLAIR was isointense for 6 (14.29%) participants (100% infectious), Hypointense for no participant, and Hyperintense for 36 (85.71%) participants (36.11% infectious, 11.11% non-infectious and 52.78% para-infectious). (Table 30 & Figure 32).

Figure 32: Bar chart special MRI sequence – FLAIR where MRI was suggestive of AES (N=42)

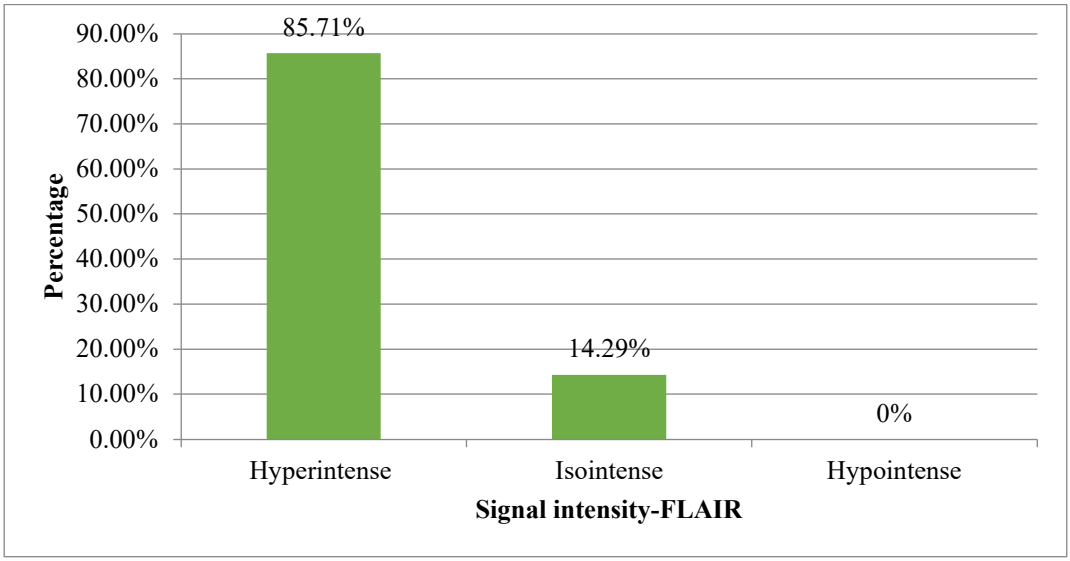


Table 31: Descriptive analysis of special MRI sequences (DWI), which shows signal intensity changes where MRI was suggestive of AES (N=42)

Signal intensity	Frequency	Percentages
Restricted diffusion	20	47.62%
Infectious	6	30%
Non-infectious	3	15%
Para infectious	11	55%
No restricted diffusion	22	52.38%
Infectious	13	59.90%
Non-infectious	1	4.54%
Para infectious	8	36.36%

Among the study population where MRI radiological findings were suggestive of AES, the signal intensity for special MRI sequence - DWI was restricted diffusion for 20 (47.62%) participants (30% infectious, 15% non-infectious, and 55% para infectious) and no restricted diffusion for 22 (52.38%) participants (59.90% infectious, 4.54% non-infectious and 36.36% para-infectious). (Table 31 & Figure 33)

Figure 33: Stacked bar chart special MRI sequence – DWI where MRI was suggestive of AES (N=42)

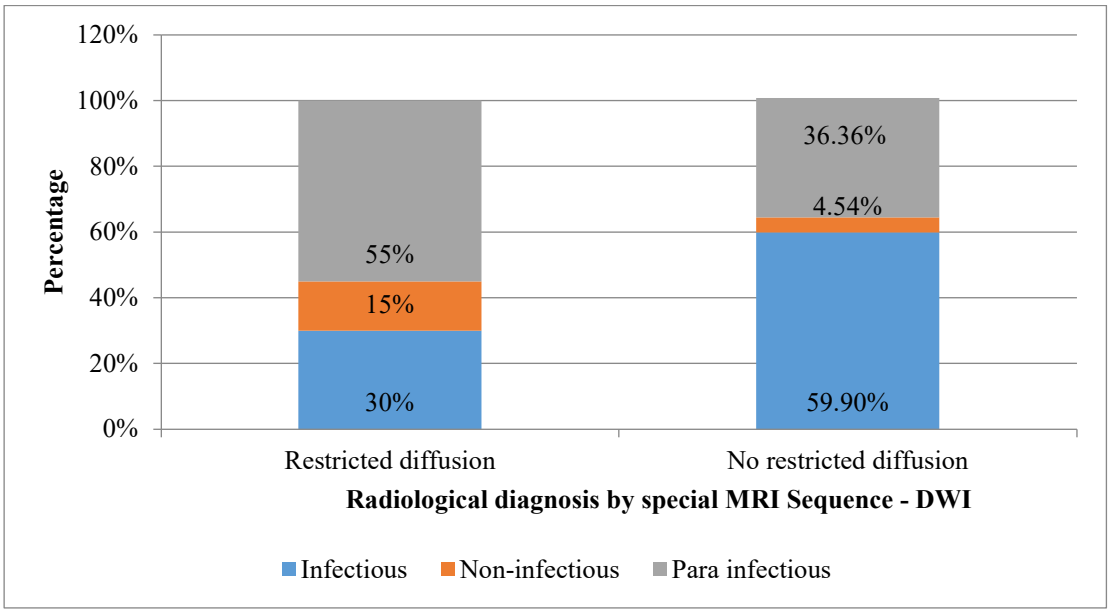


Table 32: Descriptive analysis of special MRI sequences (SWI), which shows signal intensity changes where MRI was suggestive of AES (N=42)

Signal intensity	Frequency	Percentages
Blooming	9	21.43%
Infectious	0	0%
Non-infectious	0	0%
Para infectious	9	100%
No blooming	33	78.57%
Infectious	19	57.57%
Non-infectious	4	12.12%
Para infectious	10	30.30%

Among the study population where MRI radiological findings were suggestive of AES, the signal intensity for special MRI sequence - SWI was blooming for 9 (21.43%) participants (100% para infectious) and no blooming for 33 (78.57%) participants (57.57% infectious, 12.12% non-infectious and 30.30% para-infectious). (Table 32 & Figure 34)

Figure 34: Pie chart for special MRI sequence – SWI where MRI was suggestive of AES (N=42)

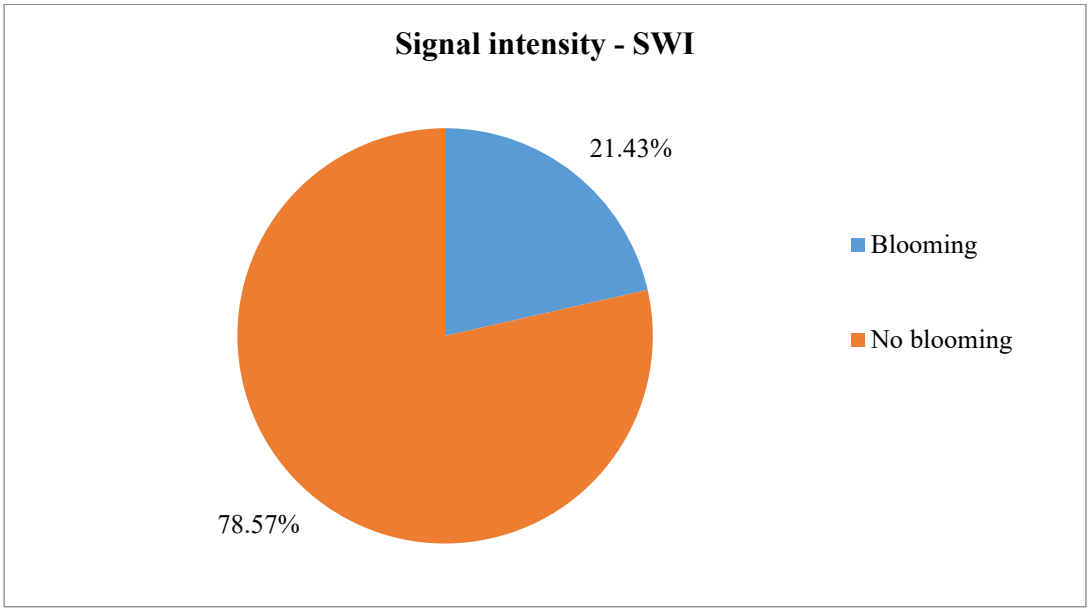


Table 33: Descriptive analysis of special MRI sequences (ADC), which shows signal intensity changes where MRI was suggestive of AES (N=42)

Signal intensity	Frequency	Percentages
Reversal on ADC maps	20	47.62%
Infectious	6	30%
Non-infectious	3	15%
Para infectious	11	55%
Non-reversal on ADC maps	22	52.38%
Infectious	13	59.90%
Non-infectious	1	4.54%
Para infectious	8	36.36%

Among the study population where MRI radiological findings were suggestive of AES, the signal intensity for special MRI sequence - ADC was a reversal on ADC maps for 20 (47.62%) participants (30% infectious, 15% non-infectious, and 55% para infectious) and non-reversal on ADC maps for 22 (52.38%) participants (59.90% infectious, 4.54% non-infectious and 36.36% para-infectious). (Table 33 & Figure 35)

Figure 35: Clustered bar chart special MRI sequence – ADC where MRI was suggestive of AES (N=42)

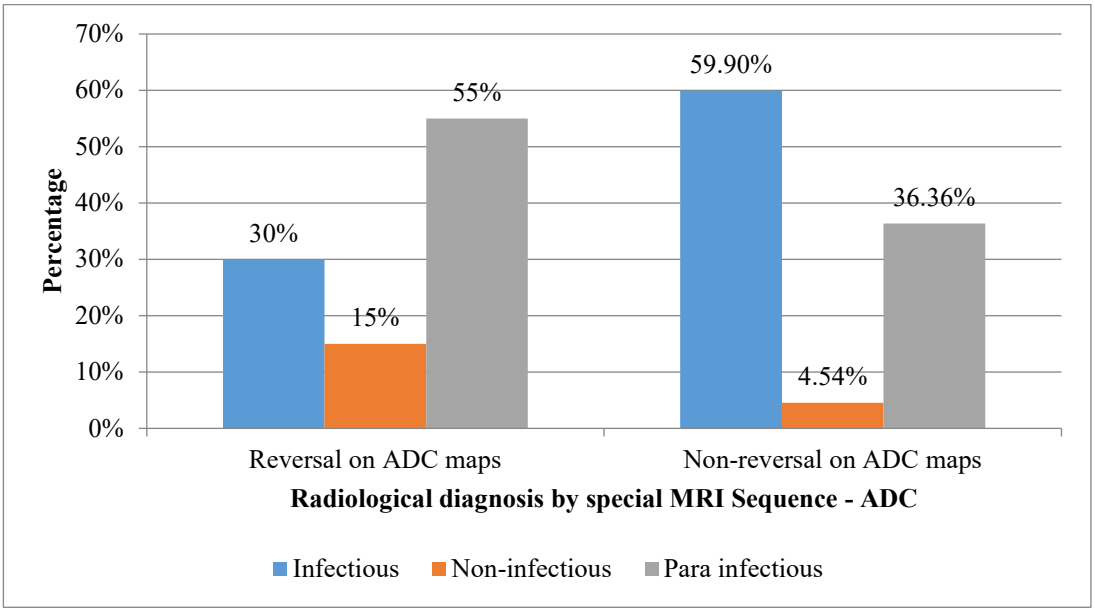
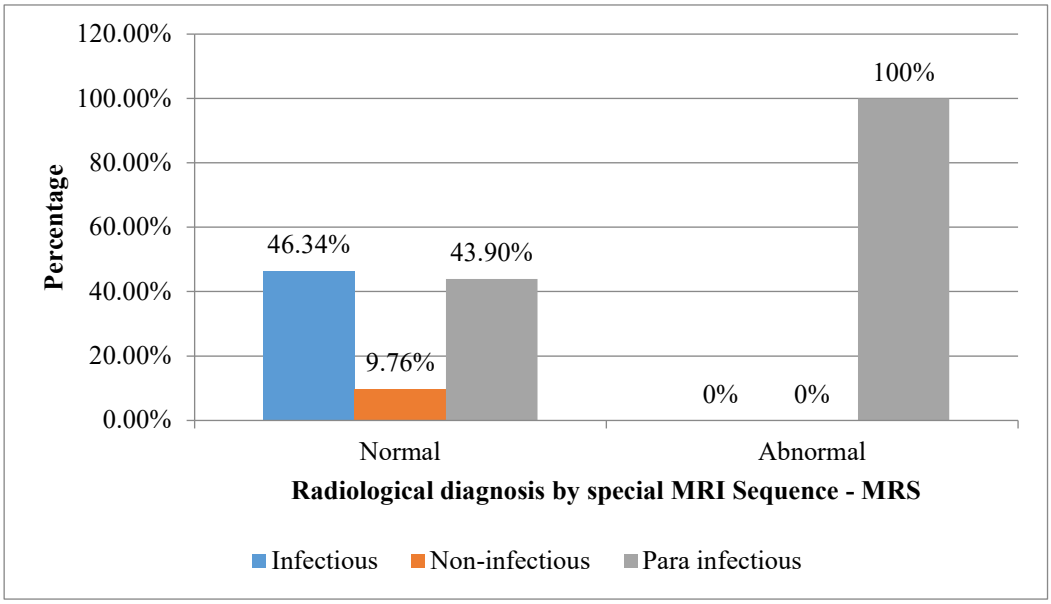


Table 34: Descriptive analysis of special MRI sequences (MRS), which shows signal intensity changes where MRI was suggestive of AES (N=42)

Signal intensity	Frequency	Percentages
Abnormal	1	2.38%
Infectious	0	0%
Non-infectious	0	0%
Para infectious	1	100%
Normal	41	97.62%
Infectious	19	46.34%
Non-infectious	4	9.76%
Para infectious	18	43.90%

Among the study population where MRI radiological findings were suggestive of AES, the signal intensity for special MRI sequence - MRS was abnormal for 1 (2.38%) participant (100% para infectious) and normal for 41 (97.62%) participants (46.34% infectious, 9.76% non-infectious and 43.90% para-infectious). (Table 34 & Figure 36)

Figure 36: Clustered bar chart special MRI sequence – MRS where MRI was suggestive of AES (N=42)



DISCUSSION:

AES is one among the major causes of mortality and morbidity in the pediatric age group. Any acute illness with fever and altered sensorium or convulsions or both come under AES.[3] Neuroimaging plays a significant role in the diagnosis and management of AES**. Evaluation with MRI Brain in different sequences can give comprehension and understanding of various etiologies of AES.**[7] The present Hospital-based observational Cross-sectional study **was done on 68 subjects aged between** 1 to 18 years with clinical features suggestive of AES, attending the Radio-diagnosis department in a tertiary care institute. **Various sequences of MRI were done with a** 3.0 Tesla MRI scanner. "T1 weighted image (T1WI), T2 weighted image (T2WI), Diffusion-Weighted Imaging (DWI), Fluid Attenuation Inversion Recovery (FLAIR), Susceptibility Weighted Imaging (SWI), Apparent Diffusion Coefficient, Magnetic Resonance Spectroscopy and Diffusion Tensor Imaging" were the MRI sequences done.

The present study is one of the pioneer studies in India, focussing on the paediatric age group, comparing various MRI sequences, including both basic and special MRI sequences in AES.

The present study is also one of its kind in exploring the yield of various MRI sequences with respect to aetiological classification by MRI. Misra UK et al.[7] in a similar study, also evaluated the role of various MRI sequences, including basic and special MRI sequences, on 88 acute viral encephalitis subjects with a 1.5 Tesla MRI scanner. The various sequences done in their study include "Axial T1WI, axial fast spin-echo T2WI, DWI, FLAIR, contrast with IV gadolinium in T1 sequence". Phukan

P et al. [36] (2021) used a 1.5 Tesla MR scanner study on serologically positive 54 JE subjects. The MRI sequences done in their study included "conventional sequences - axial T1WI, T2WI, FLAIR, DWI and SWI sequences followed by sagittal T1WI and coronal T2WI sequences. Post-gadolinium T1WI sequences in all three planes". Tripathy SK et al.[17] (2019) in their observational study, evaluated 834 clinically suspected viral AES children with basic MRI sequences. Pandit N et al. [42] (2018) did their study on 19 children with JE identified by IgM ELISA. They used the following Sequences. "DWI, coronal T2WI, axial T1WI, axial GRE/T2WI, sagittal T2WI, axial T2WI, axial FLAIR images". Sawlani V[49] (2009) evaluated 45 encephalitis cases confirmed by CSF IgM MAC-ELISA and PCR with MRI. T2W, DWI. ADC calculation and FLAIR sequences were done.

The discussion will be done under the following headings:

1. Baseline socio-demographic and clinical history of the subjects.
2. The yield of MRI in subjects suspected to have AES.
3. Clinical characteristics and aetiological classification based on MRI findings.
4. Most and least sensitive MRI Basic sequence (T1, T2) among the infectious, non-infectious, and para-infectious AES.
5. Most and least sensitive special sequence (FLAIR, DWI, ADC, SWI, MRS) among the infectious, non-infectious, and para-infectious AES.

Baseline socio-demographic and clinical history of the subjects:

The incidence of AES is high in children compared to adults.[4] 68 subjects aged between 1 to 18 years with clinically suspected AES constituted the present study sample. The majority (42.65%) were aged between 1 to 6 years. Similar to the present study, Tripathy SK et al.[17] in their study on 834 clinically suspected viral AES

children, observed the median age to be 6 years in Viral AES and 5 years in Non-viral AES. Misra UK et al.[7] observed the median age to be 24.5 years in their study. This is because they their inclusion criteria were 2 to 72 years, while the present study only included subjects less than 18 years. The majority (63.24%) of the subjects were males in the present study. Similarly, other studies also observed a higher proportion of males in their study sample.[7, 17, 36, 42] Kamble S et al.[14] (2016) in their case series of 36 AES cases in Bellary observed that majority were toddlers (30.1%) and children of pre-school age (26.5%). They also observed that male children (64.7%), children from a rural area (58.8%) were most commonly affected. With regards to the relevant clinical history, 17.65% of children were not immunized up to date, making them susceptible to infections. With regards to past medical history, 23.53% had a history of recurrent respiratory tract infections, 7.35% had a history of recurrent gastroenteritis, and 4.41% had a past history of dengue fever. In children, there is a lack of cumulative immunity derived from natural infections on comparison with adults and hence the attack rate among them is high.[15]

Table 35: Comparison of socio-demographic characteristics across the studies.

S. No	Author	Reported/ Published year	Country	Sample size and inclusion criteria	Gender (Male)	Mean age or common age group in years (yrs)
1.	Present study	2021	India	68 clinically suspected AES subjects	63.24%	42.7% between 1 to 6 yrs
2.	Phukan P et al.[36]	2021	Northeast India	54 JE subjects (serologically positive)	57.4%	mean age = 22.9 ± 1.9 yrs Range = 7 months to 73 yrs
3.	Tripathy SK et al.[17]	2019	Odisha, India	834 clinically suspected viral AES children	Males > Females	Median age 1. Viral – 6 years 2. Non-viral – 5 years
4.	Pandit N et al.[42]	2018	West Bengal, India	19 children with JE identified by IgM ELISA	57.9%	- (Inclusion criteria only available: 0 to 15 years)
5.	Misra UK et al.[7]	2010	Uttar Pradesh, India	88 clinically suspected acute viral encephalitis subjects	69.3%	Median age=24.5 years Range = 2 to 72 years
6.	Sawlani Vet al.[49]	2009	United Kingdom	45 encephalitis cases confirmed by CSF IgM MAC-ELISA and PCR	-	-

The yield of MRI in subjects suspected to have AES:

Yield is the number of cases identified by the application of a test. It can result in a good prognosis in these cases, then when identified by commonly used tests. MRI findings were suggestive of AES in 42 (61.76%) subjects. The yield of MRI was 61.76% in the present study. With regards to anatomical location involved in MRI findings suggestive of AES, the commonly involved sites were the frontal lobe (69%), temporal lobe (66.7%), and parietal lobe (64.3%). In HSV encephalitis, the temporal and frontal lobes are classically affected.[9] Pandit N et al.[42] in their study, observed Thalamic involvement was most common.

The case fatality rate is very high in AES. The aetiological diagnosis of AES is complex and is time-consuming**. MRI is time-saving as it helps in starting treatment early and supportive to the confirmatory diagnosis.** Specific MRI changes can be seen with a few pathogens.[8] Phukan P et al. [36] in their study observed that in JE, the majority had abnormalities in signal intensity in substantia nigra and bilateral thalami.

Clinical characteristics and aetiological classification based on MRI findings:

The clinical presentation and symptoms can give a clue to the diagnosis and aetiology by their characteristics such as type of rash, type of fever, associated neurological deficits, and psychiatric manifestations. AES can occur like a pure neurologic illness (JE, HSV encephalitis) or as multisystem syndrome comprising of rash, bleeding, hepatosplenomegaly (Cerebral malaria, Dengue).[23]

Among the 42 subjects with MRI suggestive of AES, 78.57% had a fever, 45.24% had convulsions, and 42.86% had limb stiffness/weakness in the present study. Misra UK et al. [7], in their study, observed that all had alteration of the sensorium, and 37 out of 88 subjects had seizures. In the present study, status epilepticus was seen in 5 subjects (11.90%). All of them had para-infectious aetiology as per MRI findings. **The** presentation can be varied depending on the site of involvement. In children, the typical symptoms could be "fever with headache and vomiting initially for a week followed by symptoms/signs of neurological deficits and/or meningeal irritation." Older children more commonly report headaches compared to young children. The severity can vary widely from being a mild illness to severe disorder presenting with neurological deficits or even death. Among those 42 subjects with MRI abnormalities suggestive of AES in the present study, 26.2% had a past history of recurrent respiratory tract infections, 11.9% had a past history of recurrent gastroenteritis, and 7.15 had a past history of dengue fever.

AES is a multifactorial clinical condition, mostly caused by viruses. The Virological diagnosis of AES is complex and is time-consuming. MRI changes and clinical presentation can give a clue to the aetiological diagnosis. The infectious agents that affect the CNS can affect by direct infection, as in encephalitis or meningitis, or indirectly through immune-mediated mechanisms or toxin-mediated reactions. The latter are grouped under para-infectious aetiology in the present study. The aetiology of AES can be broadly grouped as infective, para-infective, and non-infective categories. Among the 42 subjects with MRI suggestive of AES in the present study, the radiological diagnosis supported infectious aetiology in 45.24% (n=19), para-infectious aetiology in 45.24% (n=19), and non-infectious aetiology in 9.52% (n=4). In the present study, viral encephalitis, Japanese encephalitis, HSV

encephalitis, and encephalitis of unknown infectious aetiology were grouped under the infectious aetiology of AES. Acute necrotizing encephalitis, acute disseminated encephalomyelitis [ADEM], acute haemorrhagic leukoencephalitis, dengue encephalitis, haemorrhagic encephalitis, acute leukoencephalopathy due to rotavirus infection were grouped under Para-infectious causes of AES. Autoimmune and Rasmussen encephalitis were grouped under the Non-infectious aetiology of AES. In the present study, MRI was suggestive of ADEM in 7 subjects and of autoimmune encephalitis in 3 subjects Misra UK et al. [7] (2010) in their study observed that "22 patients had JE, 9 had dengue, 8 had herpes simplex encephalitis (HSE), 2 had Epstein-Barr virus encephalitis (EBVE), and 47 had non-specific encephalitis". Tripathy SK et al. [17], in their study, observed that "Viral etiology forms a significant proportion of pediatric AES. Morbidity and mortality are high in viral compared to nonviral AES. Herpes encephalitis (HSV-I) is the most common cause of pediatric AES in Eastern India". They also observed that prognosis was poor in Viral AES on comparison with non-viral AES.

Table 36: Distribution of AES aetiology based on MRI Brain findings (n=42)

Aetiological classification of AES by MRI (n=42)	Number (%)	Gender distribution		Age group distribution		
		Male (n=24)	Female (n=18)	1-6 years (n=19)	6-12 years (n=10)	12-18 years (n=13)
Infectious aetiology	19 (45.24%)	11 (45.83%)	8 (44.44%)	7 (36.8%)	7 (70%)	5 (38.46%)
Para-infectious aetiology	19 (45.24%)	10 (41.67%)	9 (50%)	11 (57.9%)	2 (20%)	6 (46.15%)
Non-infectious aetiology	4 (9.52%)	3 (12.5%)	1 (5.56%)	1 (5.3%)	1 (10%)	2 (15.38%)

Para-infectious aetiology was more common in the age group of 1 to 6 years (57.9%) and 12 to 18 years (46.15%), while infectious aetiology was the most common among children aged 6 to 12 years. With regards to MRI radiological findings in subjects with suspected AES but were not confirmed by MRI, 33.33% had pansinusitis. 11% had Acute leukoencephalopathy with restricted diffusion. The initial EEG may be abnormal in viral encephalitis such as HSE.[48] EEG was abnormal in 61.9% out of the 42 subjects in the present study. Abnormal EEG was more commonly seen in para-infectious (73.7%) and non-infectious AES (75%) than infectious AES.

Table 37: Comparison of the yield of basic and special MRI sequences for AES.

Aetiological classification of AES by MRI	T1	T2	FLAIR	DWI	ADC	SWI	MRS
Infectious AES	21%	89.5%	68.4%	31.6%	36.8%	-	-
Para-infectious AES	63.2%	100%	100%	75%	57.9%	47.4%	5.3%
Non-infectious AES	75%	100%	100%	57.9%	75%	-	-

Most and least sensitive MRI Basic sequence (T1, T2) among the infectious, non-infectious, and para-infectious AES:

Among the basic sequences, the yield of T2 was better than T1 in the present study. The yield of T2 was 100% for para-infectious and non-infectious AES. It was 89.5% for infectious AES. The yield of T1 was very lower at 21% for infectious AES, 75% for non-infectious AES, and 63.2% for para-infectious AES.

In the basic T1 sequence, the Hypointense signal was the predominant signal in para-infectious and non-infectious AES. T1 was isointense for 79% in infectious AES, 63.2% in para-infectious AES, and 75% in non-infectious AES. In the basic T2 sequence, the Hyperintense signal was the most predominant signal in all types of AES. T2 was hyperintense for 89.5% in infectious AES, 100% in both para-infectious and non-infectious AES.

Similarly, Misra UK et al.[7] in their study, observed that T2 sequences were the more sensitive basic sequence in revealing abnormalities in viral encephalitis. Tripathy SK et al.[17] in their study, observed high-intensity temporal lobe lesions on

T2-WI in HSV-I infection. Pandit N et al.[42] in their study on subjects with JE, observed that hyperintensity in T2/FLAIR images was less marked on comparison with DWI images. Thalamic hyperintensities in T2WI are highly specific for JE in areas that are endemic for JE.[36] Global involvement is more common in HSV-II infection.[17] In JE, limbic area involvement is more common compared to global cerebral involvement. Only global involvement is seen In varicella-zoster virus infection.[17]

Most and least sensitive special sequence (FLAIR, DWI, ADC, SWI, MRS) among the infectious, non-infectious, and para-infectious AES:

With regards to special sequences, FLAIR was the most sensitive in picking up abnormalities. The yield of FLAIR was best (100%) for non-infectious and para-infectious AES. With regards to infectious AES, the yield was only 68.4%. But it was the best among all the special sequences. The yield of DWI was very lower at 31.6% for infectious AES and 576.95 for non-infectious AES compared to the other special sequences. The yield of ADC was very lower at 57.9% for para-infectious AES compared to FLAIR and DWI. SWI and MRS were not significant for any subject with infectious and non-infectious AES. With regards to para-infectious AES, the yield of SWI was 47.4%, and MRS was 5.3%.

Misra UK et al.[7] (2010), in their study, also observed that "MRI abnormalities were more common in FLAIR (57.1%) compared to T2 (52.9%), DWI (38.1%) and T1 (19.3%) sequences". They observed that FLAIR was the most sensitive special sequence. They also observed that, on comparison with dengue and non-specific encephalitis, changes in MRI were commonly seen in Acute viral encephalitis.

Hyperintense signal was the predominant finding in FLAIR observed in 85.7% of subjects. Blooming was observed in 21.4% of subjects in the SWI sequence in the present study. Restricted diffusion was observed in 47.6% of subjects in the DWI sequence, while reversal on ADC maps was observed in 47.6 % of subjects. Misra UK et al.[7] (2010), in their study, observed that mean ADC was lower in JE compared to HSE. Phukan P et al.[36] in their study, observed that DWI with ADC mapping has the potential to determine JE staging. Pandit N et al.[42] in their study on JE subjects, observed that Hyper intensity in T2/FLAIR images was less marked on comparison with DWI images. Sawlani V et al.[49] also observed significant differences in restricted diffusion and ADC values between acute and chronic stages of JE and also in HSE.

It can be concluded based on the present study findings that T2WI was the most sensitive basic sequence while FLAIR was the most sensitive special sequence in clinically suspected patients undergoing MRI. The yield of MRI was good at 61.76%.

CONCLUSIONS:

1. AES is a multifactorial clinical condition, mostly caused by viruses
2. Virological diagnosis is complex. MRI is **time-saving as it helps in starting treatment early and supportive to the confirmatory diagnosis.**
3. The present study was carried on 68 subjects aged between 1 to 18 years. The majority (42.65%) were aged between 1 to 6 years. The majority (63.24%) were males
4. 17.65% of the children were not immunized up to date. 23.53% had a history of recurrent respiratory tract infections, 7.35% had a history of recurrent gastroenteritis, 4.41% had a past history of dengue fever.
5. The yield of MRI was 61.76% (42 out of 68 subjects).
6. Among them, the majority (54.1%, n=24) were males. 11 (26.19%) had a past history of recurrent respiratory tract infections, 5 had a past history of recurrent gastroenteritis (11.9%), and 3 had a past history of dengue fever (7.14%).
7. Among the 42 subjects with MRI suggestive of AES, 78.57% had a fever, 45.24% had convulsions, 42.86% had limb stiffness/weakness.
8. EEG was abnormal in 61.9% out of the 42 subjects in the present study.

9. Among the 42 subjects with MRI suggestive of AES, the radiological diagnosis supported infectious aetiology in 45.24% (n=19), para-infectious aetiology in 45.24% (n=19) and non-infectious aetiology in 9.52% (n=4).
10. Para-infectious aetiology was more common among children aged 1 to 6 years (57.9%) and 12 to 18 years (46.15%), while infectious aetiology was the most common among children aged 6 to 12 years.
11. With regards to anatomical location involved in MRI suggestive of AES (N=42), the commonly involved sites were the frontal lobe (69%), temporal lobe (66.7%), and parietal lobe (64.3%).
12. MRI was suggestive of ADEM in 7 subjects. Out of these, one was positive for Anti MOG antibody.
13. MRI was suggestive of autoimmune encephalitis in 3 subjects. Out of these, none were positive for Anti MOG antibody.
14. Among the basic sequences in the present study, the yield of T2 was better than T1. The yield of T2 was 100% for para-infectious and non-infectious AES. It was 89.5% for infectious AES. The yield of T1 was very lower at 21% for infectious AES, 75% for non-infectious AES, and 63.2% for para-infectious AES.
15. T2 was hyperintense for 89.5% in infectious AES, 100% in both para-infectious and non-infectious AES.

16. With regards to special sequences, FLAIR was the most sensitive in picking up abnormalities. The yield of FLAIR was best (100%) for non-infectious and para-infectious AES. With regards to infectious AES, the yield was only 68.4%. But it was the best among all the special sequences.
17. The yield of DWI was very lower at 31.6% for infectious AES and 57.95 for non-infectious AES compared to the other special sequences.
18. The yield of ADC was very lower at 57.9% for para-infectious AES compared to FLAIR and DWI.
19. SWI and MRS findings were not significant for any subject with infectious and non-infectious AES. With regards to para-infectious AES, the yield of SWI was 47.4%, and MRS was 5.3%.
20. Hyperintense signal was the predominant finding in FLAIR observed in 85.7% of subjects. Blooming was observed in 21.4% of subjects in the SWI sequence in the present study. Restricted diffusion was observed in 47.6% of subjects in the DWI sequence, while reversal on ADC maps was observed in 47.6 % of subjects.
21. T2 WI was the most sensitive basic sequence, while FLAIR was the most sensitive special sequence in clinically suspected patients undergoing MRI.

LIMITATIONS AND RECOMMENDATIONS:

The cross-sectional nature of the study and the single Centre sample recruitment affects the validity of the present study findings and its generalizability. The non-probability sampling technique use for the requirement is also a limitation. But the present study is one of its kind in the present study area comparing various MRI sequences with respect to an aetiological basis in AES. Large-scale, multi-centric prospective studies in the future incorporating the evaluation of outcome and validity of MRI sequences in predicting the outcome are recommended.

SUMMARY:

Acute Encephalitis Syndrome (AES) is defined as an acute onset of fever with a change in mental status presenting as confusion or altered sensorium or coma or new onset of seizures (excluding febrile seizure). AES is a multifactorial clinical entity, mostly caused by viruses. The etiology in a major number of AES cases still remains unclear. The season and geographical location seem to have an influence regarding the causative agents of AES, which predominantly affects pediatric age groups below 15 years. MRI evaluation of the brain with the utilization of its basic and special MRI sequences gives a comprehensive understanding of various etiologies of AES. Time-saving is MRI as it helps in early treatment administration and supportive care in the suspected cases. In patients with AES, the findings of Neuroimaging can be quiet different or normal. The MRI of the brain with and without contrast using T1-weighted, T2-weighted, diffusion-weighted imaging, susceptibility-weighted imaging, and fluid-attenuated inversion recovery (FLAIR) sequences is the modality of choice in assessing the changes consistent with inflammation of brain parenchyma as specific MRI changes can be characteristically seen with a few pathogens. Hence, the present study was done to estimate the yield of MRI in patients suspected to have AES and to compare of various MRI sequences in AES patients.

The present Hospital-based observational Cross-sectional study was done on 68 subjects aged between 1 to 18 years with clinical features suggestive of AES, attending the Radio-diagnosis department in a tertiary care institute. Various sequences of MRI were done with a 3.0 Tesla MRI scanner. T1 weighted image (T1WI), T2 weighted image (T2WI), Diffusion-Weighted Imaging (DWI), Fluid

Attenuation Inversion Recovery (FLAIR), Susceptibility Weighted Imaging (SWI), Apparent Diffusion Coefficient and Magnetic Resonance Spectroscopy were the MRI sequences done. For the continuous quantitative variables, mean and standard deviation were calculated. The categorical data were presented as rate, ratio, and proportion. For all the tests, the value of p less than 5% (0.05) was considered significant. Suitable graphs were used to depict the comparison. Data were analyzed by using SPSS software, V.22.

The majority (42.65%) were aged between 1 to 6 years. The majority were males (63.24%). The yield of MRI was 61.76% (42 out of 68 subjects). Among the 42 subjects with MRI suggestive of AES, the radiological diagnosis supported infectious aetiology in 45.24% (n=19), para-infectious aetiology in 45.24% (n=19) and non-infectious aetiology in 9.52% (n=4). With regards to anatomical location involved in MRI suggestive of AES (N=42), the commonly involved sites were the frontal lobe (69%), temporal lobe (66.7%), and parietal lobe (64.3%). Among the basic sequences in the present study, the yield of T2 was better than T1. The yield of T2 was 100% for para-infectious and non-infectious AES. It was 89.5% for infectious AES. The yield of T1 was very lower at 21% for infectious AES, 75% for non-infectious AES, and 63.2% for para-infectious AES. With regards to special sequences, FLAIR was the most sensitive in picking up abnormalities. The yield of FLAIR was best (100%) for non-infectious and para-infectious AES. With regards to infectious AES, the yield was only 68.4%. But it was the best among all the special sequences. The yield of DWI was very lower at 31.6% for infectious AES and 57.95 for non-infectious AES compared to the other special sequences. The yield of ADC was very lower at 57.9% for para-infectious AES compared to FLAIR and DWI. SWI and MRS findings were

not significant for any subject with infectious and non-infectious AES. With regards to para-infectious AES, the yield of SWI was 47.4%, and MRS was 5.3%.

It can be concluded based on the present study findings that T2WI was the most sensitive basic sequence while FLAIR was the most sensitive special sequence in clinically suspected patients undergoing MRI. The yield of MRI was good at 61.76%.

The cross-sectional nature of the study and the single Centre sample recruitment affects the validity of the present study findings and its generalizability. The non-probability sampling technique use for the requirement is also a limitation. But the present study is one of its kind in the present study area comparing various MRI sequences with respect to an aetiological basis in AES. Large-scale, multi-centric prospective studies in the future incorporating the evaluation of outcome and validity of MRI sequences in predicting the outcome are recommended.

BIBLIOGRAPHY

1. Sharma S, Mishra D, Aneja S, Kumar R, Jain A, Vashishtha VM, et al. Consensus guidelines on evaluation and management of suspected acute viral encephalitis in children in India. Indian Pediatr. 2012;49(11):897-910.
2. Joshi R, Kalantri SP, Reingold A, Colford JM Jr. Changing landscape of acute encephalitis syndrome in India: a systematic review. Natl Med J India. 2012;25(4):212-20. .
3. World Health Organization. Surveillance standards for vaccine-preventable diseases, 2nd edition. 2018. Accessed on 20/06/2021. Availbale from: https://www.who.int/publications/i/item/surveillance-standards-for-vaccine-preventable-diseases-2nd-edition.
4. Granerod J, Crowcroft NS. The epidemiology of acute encephalitis. Neuropsychol Rehabil. 2007;17(4-5):406-28.
5. World Health Organization. Japanese Encephalitis. 2019. Accessed on 20/06/2021. Availbale from: https://www.who.int/news-room/fact-sheets/detail/japanese-encephalitis.
6. Tiwari S, Singh RK, Tiwari R, Dhole TN. Japanese encephalitis: a review of the Indian perspective. Braz J Infect Dis. 2012;16(6):564-73.
7. Misra UK, Kalita J, Phadke RV, Wadwekar V, Boruah DK, Srivastava A, et al. Usefulness of various MRI sequences in the diagnosis of viral encephalitis. Acta Trop. 2010;116(3):206-11.
8. Kumar R. Understanding and managing acute encephalitis. F1000Res. 2020;9.
9. Ajithkumar AK, Mendez MD. Herpes Simplex Encephalitis. [Updated 2021 Feb 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing;

2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557643/.

10. Erlanger TE, Weiss S, Keiser J, Utzinger J, Wiedenmayer K. Past, present, and future of Japanese encephalitis. Emerg Infect Dis. 2009;15(1):1-7.
11. National Health Portal, India. Acute encephalitis syndrome. Accessed on 19/06/2021. Available at: https://www.nhp.gov.in/disease/communicable-disease/acute-encephalitis-syndrome.
12. Ghosh S, Basu A. Acute Encephalitis Syndrome in India: The Changing Scenario. Ann Neurosci. 2016;23(3):131-3.
13. Narain JP, Dhariwal AC, MacIntyre CR. Acute encephalitis in India: An unfolding tragedy. Indian J Med Res. 2017;145(5):584-587.
14. Kamble S, Raghvendra B. A clinico-epidemiological profile of acute encephalitis syndrome in children of Bellary, Karnataka, India. Int J Community Med Public Health. 2016;3(11):2997-3002.
15. Ministry of Health and Family Welfare. National Programme for Prevention and Control of Japanese Encephalitis/Acute Encephalitis Syndrome, Operational Guidelines. New Delhi:National Vector Borne Disease Control Programme, Directorate General of Health Services, Ministry of Health and Family Welfare; 2014.
16. Tiwari JK, Malhotra B, Chauhan A, Malhotra H, Sharma P, Deeba F, et al. Aetiological study of viruses causing acute encephalitis syndrome in North West India. Indian J Med Microbiol. 2017;35(4):529-34.
17. Tripathy SK, Mishra P, Dwibedi B, Priyadarshini L, Das RR. Clinico-epidemiological Study of Viral Acute Encephalitis Syndrome Cases and

Comparison to Nonviral Cases in Children from Eastern India. J Glob Infect Dis. 2019;11(1):7-12.

18. Kumar R. Encephalitis & Encephalopathies in Medical Emergencies in Children.Ed Singh M,. Fifth edition. Sagar Publications. New Delhi.2012;324–32.
19. Michael BD, Griffiths MJ, Granerod J, Brown D, Davies NW, Borrow R, et al. Characteristic Cytokine and Chemokine Profiles in Encephalitis of Infectious, Immune-Mediated, and Unknown Aetiology. PLoS One. 2016;11(1):e0146288.
20. Grahn A, Studahl M. Varicella-zoster virus infections of the central nervous system - Prognosis, diagnostics and treatment. J Infect. 2015;71(3):281-93.
21. Baruah HC, Biswas D, Patgiri D, Mahanta J. Clinical outcome and neurological sequelae in serologically confirmed cases of Japanese encephalitis patients in Assam, India. Indian Pediatr. 2002;39(12):1143-8.
22. Cherry JD: Encephalitis. In: Nelson Textbook of Pediatrics Behrman RE, Kleigman RM (Eds.). WB Saunders Co, Pennsylvania, 14thedn1993;666–669.
23. Misra UK, Mani VE, Kalita J. A Cost-Effective Approach to the Diagnosis and Management of Acute Infectious Encephalitis. Eur Neurol. 2017;77(1-2):66-74.
24. Venkatesan A, Geocadin RG. Diagnosis and management of acute encephalitis: A practical approach. Neurol Clin Pract. 2014;4(3):206-15.
25. Kennard C, Swash M. Acute viral encephalitis: its diagnosis and outcome. Brain. 1981;104(Pt 1):129-48.

26. Said S, Kang M. Viral Encephalitis. [Updated 2020 Aug 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470162/.

27. Glaser CA, Honarmand S, Anderson LJ, Schnurr DP, Forghani B, Cossen CK, et al. Beyond viruses: clinical profiles and etiologies associated with encephalitis. Clin Infect Dis. 2006;43(12):1565-77.

28. Saxena V, Mishra VK, Dhole TN. Evaluation of reverse-transcriptase PCR as a diagnostic tool to confirm Japanese encephalitis virus infection. Trans R Soc Trop Med Hyg. 2009;103(4):403-6.

29. Sarkar A, Taraphdar D, Mukhopadhyay SK, Chakrabarti S, Chatterjee S. Molecular evidence for the occurrence of Japanese encephalitis virus genotype I and III infection associated with acute encephalitis in patients of West Bengal, India, 2010. Virol J. 2012;9:271.

30. Misra UK, Kalita J. Neurophysiological studies in herpes simplex encephalitis. Electromyogr Clin Neurophysiol. 1998;38(3):177-82.

31. Sankaranarayanan M, Shah S, Thomas P, Kannoth S, Radhakrishnan K. Persistent extreme delta brush in anti-NMDA-receptor encephalitis: Does it portend a poor prognosis? Epilepsy Behav Rep. 2019;12:100324.

32. Navin P, Delanty N, Brennan P, Looby S. Herpes simplex virus encephalitis involving the right thalamus. BMJ Case Rep. 2013;2013.

33. Misra UK, Kalita J, Jain SK, Mathur A. Radiological and neurophysiological changes in Japanese encephalitis. J Neurol Neurosurg Psychiatry. 1994;57(12):1484-7.

34. Lu SJ, Goh PS. Isolated temporal lobe involvement in Japanese encephalitis. J Neuroimaging. 2009;19(3):280-2.

35. Handique SK, Das RR, Barman K, Medhi N, Saharia B, Saikia P, Ahmed SA. Temporal lobe involvement in Japanese encephalitis: problems in differential diagnosis. AJNR Am J Neuroradiol. 2006;27(5):1027-31.

36. Phukan P, Sarma K, Sharma BK, Boruah DK, Gogoi BB, Chuunthang D. MRI Spectrum of Japanese Encephalitis in Northeast India: A Cross-Sectional Study. J Neurosci Rural Pract. 2021;12(2):281-9.

37. Lancaster E. The Diagnosis and Treatment of Autoimmune Encephalitis. J Clin Neurol. 2016;12(1):1-13.

38. Armangue T, Leypoldt F, Dalmau J. Autoimmune encephalitis as differential diagnosis of infectious encephalitis. Curr Opin Neurol. 2014;27(3):361-8.

39. Gujar SK, Maheshwari S, Bjorkman-Burtscher I, Sundgren PC. Magnetic resonance spectroscopy. J Neuroophthalmol. 2005;25(3):217-26.

40. Tognarelli JM, Dawood M, Shariff MI, Grover VP, Crossey MM, Cox IJ, et al. Magnetic Resonance Spectroscopy: Principles and Techniques: Lessons for Clinicians. J Clin Exp Hepatol. 2015;5(4):320-8.

41. Ghosh MK IK, Datta AK, Roy A, Das R, Seth S. Study on the Assessment of Clinical & Neuroimaging Features of Acute Encephalitis Syndrome & Their Prognostic Significance among Children Admitted in the Pediatric Emergency Ward of Burdwan Medical College, Burdwan. J Pediatr Assoc India. 2018;7(1):23.

42. Pandit N, Roy AC, Mustafa Z. Predominant areas of brain involved in children [0 to 15 yrs] with Japanese encephalitis by MRI study. J Evid Based Healthc. 2018;5(31):2324-2329.

43. James J, Johnson J, Jose J, Nk T. Herpes Simplex Virus Encephalitis in a Healthy Lady. Journal of Rare Disorders: Diagnosis & Therapy. 2018;04(03).

44. Jain P, Prakash S, Khan DN, Garg RK, Kumar R, Bhagat A, Ramakrishna V, Jain A. Aetiology of acute encephalitis syndrome in Uttar Pradesh, India from 2014 to 2016. J Vector Borne Dis. 2017;54:311-6.

45. Jayaraman K, Rangasami R, Chandrasekharan A. Magnetic Resonance Imaging Findings in Viral Encephalitis: A Pictorial Essay. J Neurosci Rural Pract. 2018;9(4):556-60.

46. Bykowski J, Kruk P, Gold JJ, Glaser CA, Sheriff H, Crawford JR. Acute pediatric encephalitis neuroimaging: single-institution series as part of the California encephalitis project. Pediatr Neurol. 2015;52(6):606-14.

47. Songmen S PO, Maharjan S, Paudel S, Ansari MA, Ghimire RK. A Retrospective Study of Magnetic Resonance Imaging Findings in Acute Encephalitis Syndrome. Journal of Institute of Medicine. 2015;2(2).

48. Rozenberg F. Acute viral encephalitis. Handb Clin Neurol. 2013;112:1171-81.

49. Sawlani V. Diffusion-weighted imaging and apparent diffusion coefficient evaluation of herpes simplex encephalitis and Japanese encephalitis. J Neurol Sci. 2009;287(1-2):221-6.

50. Misra UK, Kalita J, Srivastav A, Pradhan PK. The prognostic role of magnetic resonance imaging and single-photon emission computed tomography in viral encephalitis. Acta Radiol. 2008;49(7):827-32.

51. SPSS I. IBM SPSS Statistics Version 22 Statistical Software: Core System Users' Guide. SPSS Inc. 2014.

ANNXURE I - INFORMED CONSENT

KAHER

JAWAHARLAL NEHRU MEDICAL COLLEGE, BELAGAVI

DEPARTMENT OF RADIODIAGNOSIS

TITLE OF THE STUDY: "MAGNETIC RESONANCE IMAGING EVALUATION OF ACUTE ENCEPHALITIS SYNDROME IN PEDIATRIC PATIENTS IN A TERTIARY CARE HOSPITAL – A CROSS-SECTIONAL STUDY"

PRINCIPAL INVESTIGATOR: _____

GUIDE: _____

INTRODUCTION AND PURPOSE:

PROCEDURE:

I request you to kindly participate in the study titled study **"MAGNETIC RESONANCE IMAGING EVALUATION OF ACUTE ENCEPHALITIS SYNDROME IN PEDIATRIC PATIENTS IN A TERTIARY CARE HOSPITAL – A CROSS-SECTIONAL STUDY"** at Dr. Prabhakar Kore charitable hospital and Medical Research Centre, Belagavi" is being conducted by _____ post-graduate in Radiodiagnosis at J. N. Medical College Belgaum, Karnataka, under the guidance of _____, Professor, Dept. of Radiodiagnosis, J. N. Medical College, Belagavi.

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. You 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 multi-parametric MR imaging of the central nervous system conducted earlier.

ALTERNATIVES:

If the patient is not willing to take part in the study, his / her treatment or any other further investigations the patient wants to undergo, in the 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 an investigation for acute encephalitis syndrome by the referring consultant, and the participants will bear the charges for it.)

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

COMPENSATION:

In the event that I become injured as a result of taking part in this study, whatever treatment 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:

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

Dr. Roopa Bellad
Professor Chairman, J.N. Medical College Institutional Ethical Committee For Human Subjects Research, Belagavi
Ph. No: 0831-2473777, Ext. 1529

CONSENT TO PARTICIPATE IN RESEARCH STUDY:

1. I understand that I am participating in the study, which includes multi-parametric Magnetic Resonance Imaging of the central nervous system.

2. I confirm that I have read and understood the information in the patient information sheet. The 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 is 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 _____

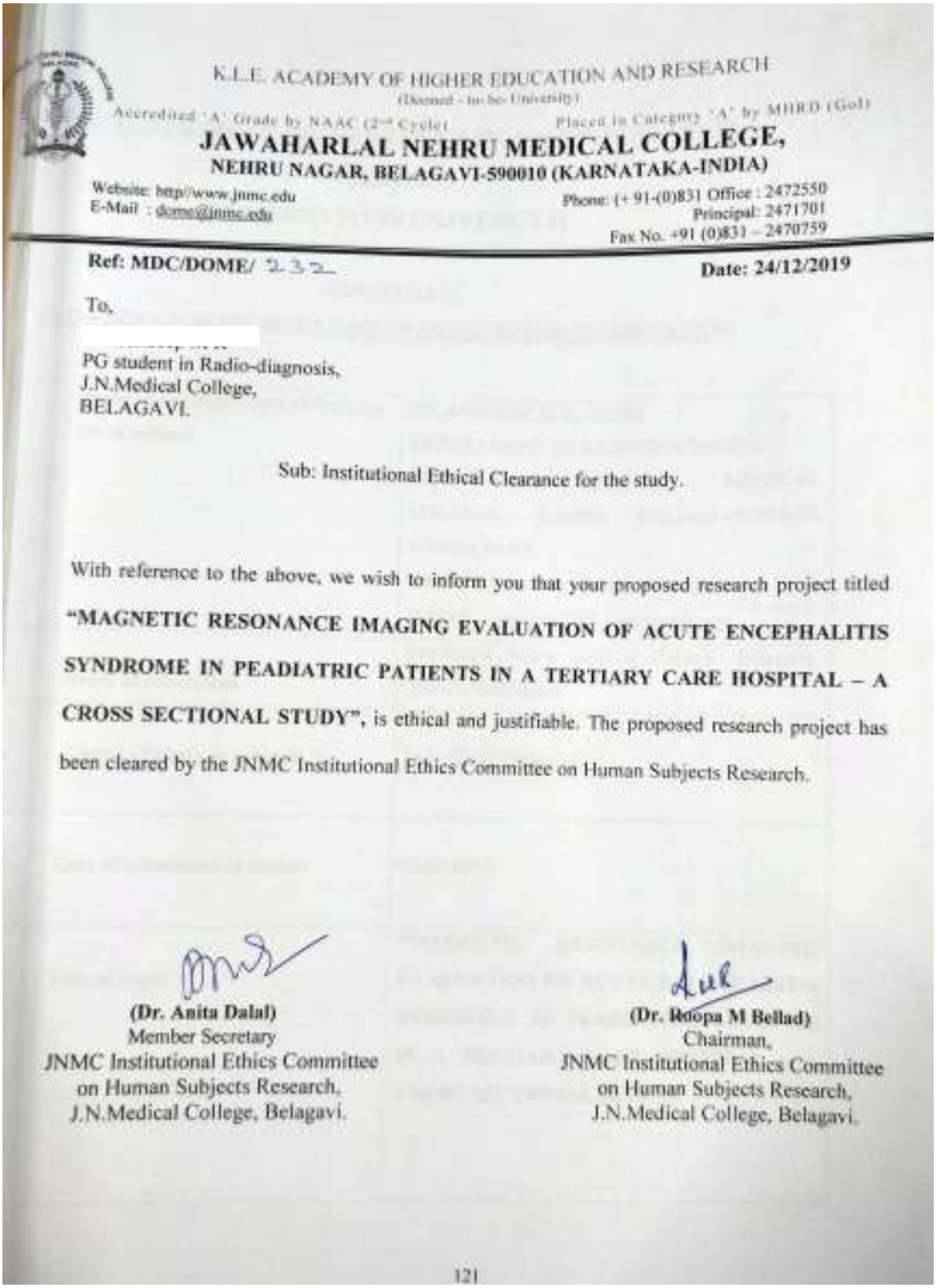
Name and signature of witness _____

Name and signature of interviewer _____

Date:

Place:

ANNEXURE II – ETHICAL CLEARANCE



K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed - to-be University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)

JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)

Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu

Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 232 **Date: 24/12/2019**

To,

PG student in Radio-diagnosis,
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 **"MAGNETIC RESONANCE IMAGING EVALUATION OF ACUTE ENCEPHALITIS SYNDROME IN PEADIATRIC PATIENTS IN A TERTIARY CARE HOSPITAL – A CROSS SECTIONAL STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Anita Dalal)
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.

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ANNEXURE III- PROFORMA

JAWAHARLAL NEHRU MEDICAL COLLEGE, BELAGAVI
DEPARTMENT OF RADIODIAGNOSIS

PROFORMA FOR DATA COLLECTION

NAME_____

AGE_____ **OP/IP NO** _____

MOBILE NO._____

ADDRESS _____

_____

MRI NUMBER: _____

CHIEF COMPLAINTS: **1.**
2.
3.

HISTORY OF PRESENTING ILLNESS:

BIRTH HISTORY:

DEVELOPMENTAL HISTORY:

IMMUNISATION HISTORY:

PAST HISTORY:

FAMILY HISTORY:

CLINICAL EXAMINATION:

CENTRAL NERVOUS SYSTEM:

CARDIOVASCULAR SYSTEM:

RESPIRATORY SYSTEM:

PER ABDOMINAL EXAMINATION:

PROVISIONAL DIAGNOSIS:

MRI REPORT:

BRAIN AREAS	**SEQUENCES**						
	T1	**T2**	**FLAIR**	**DWI**	**ADC**	**SWI**	**MRS**
1.CEREBRUM **-FRONTAL LOBE** • **CORTEX** • **SUBCORTICAL WHITE MATTER** • **DEEP WHITE MATTER** **-PARIETAL LOBE** • **CORTEX** • **SUBCORTICAL WHITE MATTER** • **DEEP WHITE MATTER** **-TEMPORAL LOBE** • **CORTEX** • **SUBCORTICAL WHITE MATTER** • **DEEP WHITE MATTER** **-OCCIPITAL LOBE** • **CORTEX** • **SUBCORTICAL WHITE MATTER** • **DEEP WHITE MATTER** **-CENTRUM SEMIOVALE** **-CORONA RADIATA** **-CORPUS CALLOSUM** **-BASAL GANGLIA** • **CAUDATE NUCLEUS** • **LENTIFORM NUCLEUS** **a) PUTAMEN** **b) GLOBUS PALLIDUS** **c) SUBTHALAMIC NUCLEUS** **d) SUBSTANTIA NIGRA**							

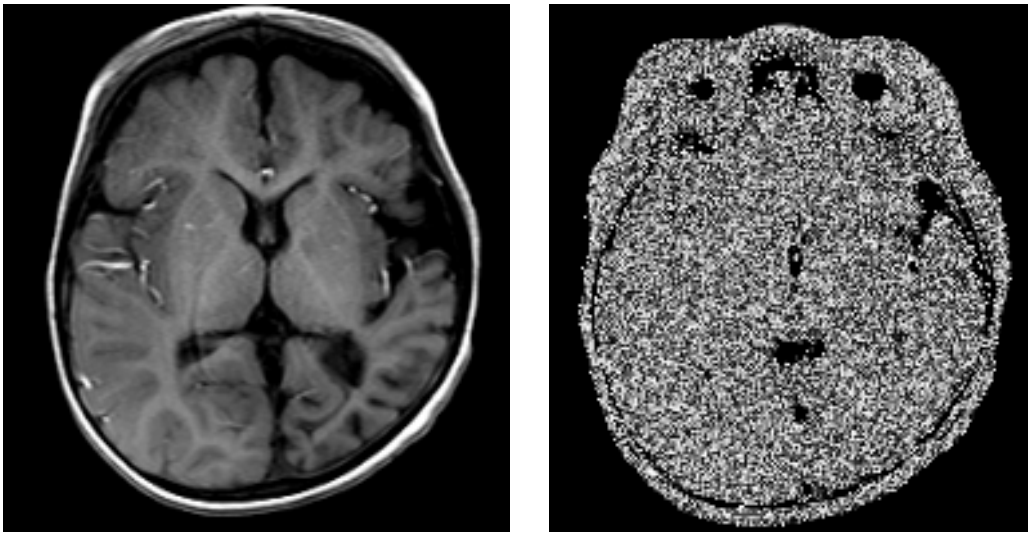
-CEREBELLUM • **CEREBELLAR HEMISPHERES** • **MEDIAN VERMIS** **-MID BRAIN:** **a) -THALAMUS** **b) -TECTUM** **c) -TEGMENTUM** **d) -CEREBRAL PEDUNCLES** **e) CORPORA QUADRIGEMINA** **f) POSTERIOR PERFORATED SUBSTANCE** **g) PERIAQUEDUCTAL GREY** **-PONS** **-MEDULLA OBLONGATA**								

FINAL DIAGNOSIS:

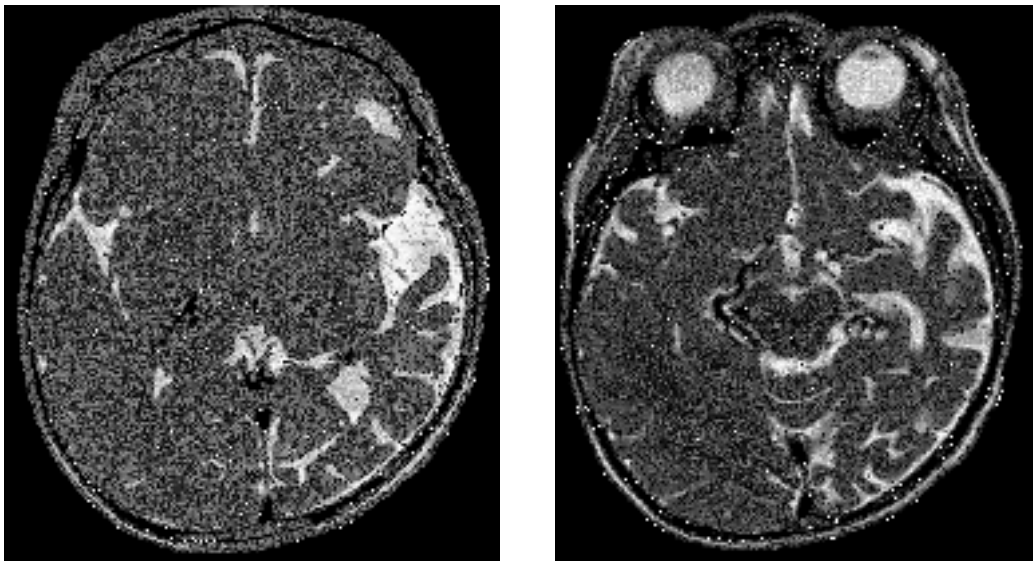
ANNEXURE IV- PHOTOGRAPHS

Figure 37: Description and radiological images of a case of Rasmussen's encephalitis.

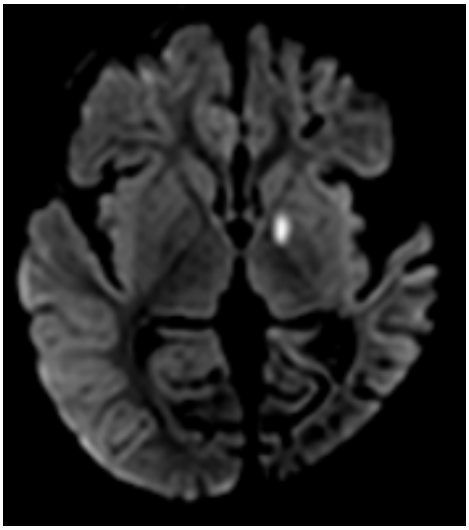
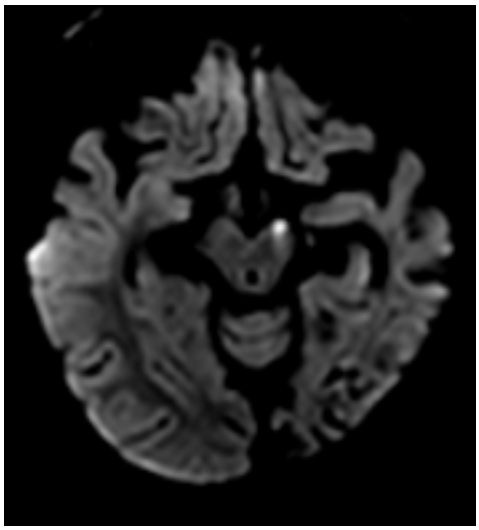
Case 1: a 2 year of the female patient came with weakness of the right upper and lowered limbs for 5 days with 3 episodes of convulsions. Her CSF showed pleocytosis; however, her EEG was normal at the time of presentation. The MRI of her brain revealed T2 & FLAIR hyperintense and T1 hypointense areas, which showed diffusion restriction on DWI sequence in the left globus pallidus, posterior limb of the left internal capsule, and left crus cerebri. There was unilateral cortical atrophy with prominent sulci, Sylvian fissure, and subarachnoid spaces on the left side with mild prominence of body, atria, and the occipital horn of left lateral ventricle.



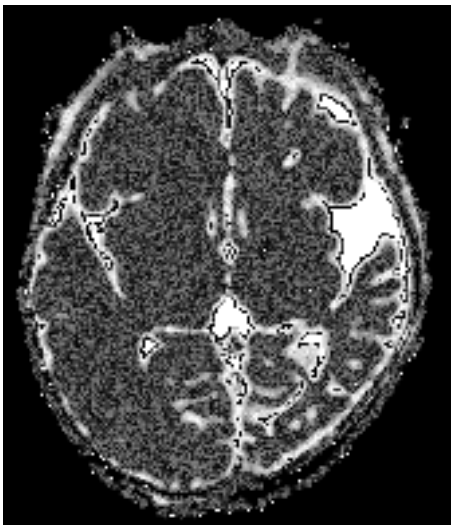
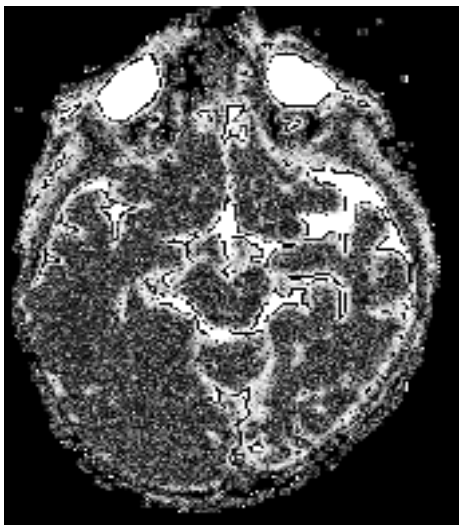
T1 sequence axial



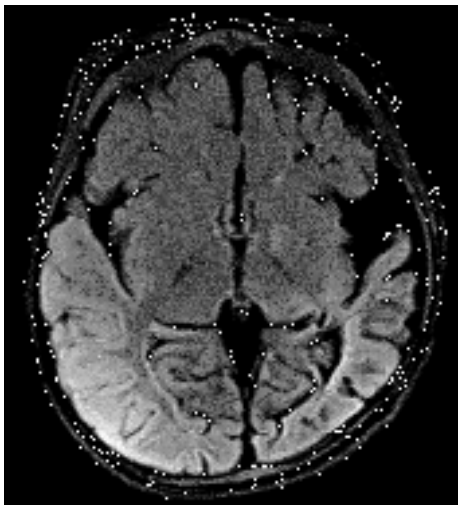
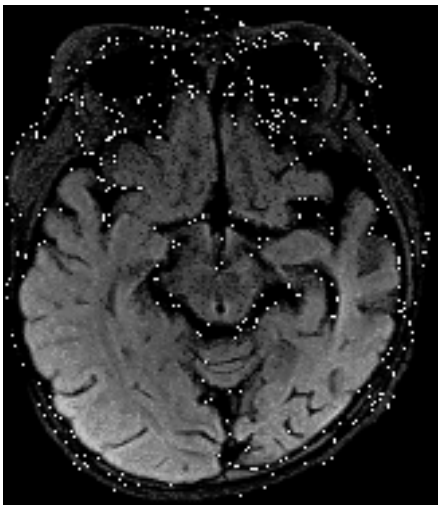
T2 sequence axial

DW1 sequence axial

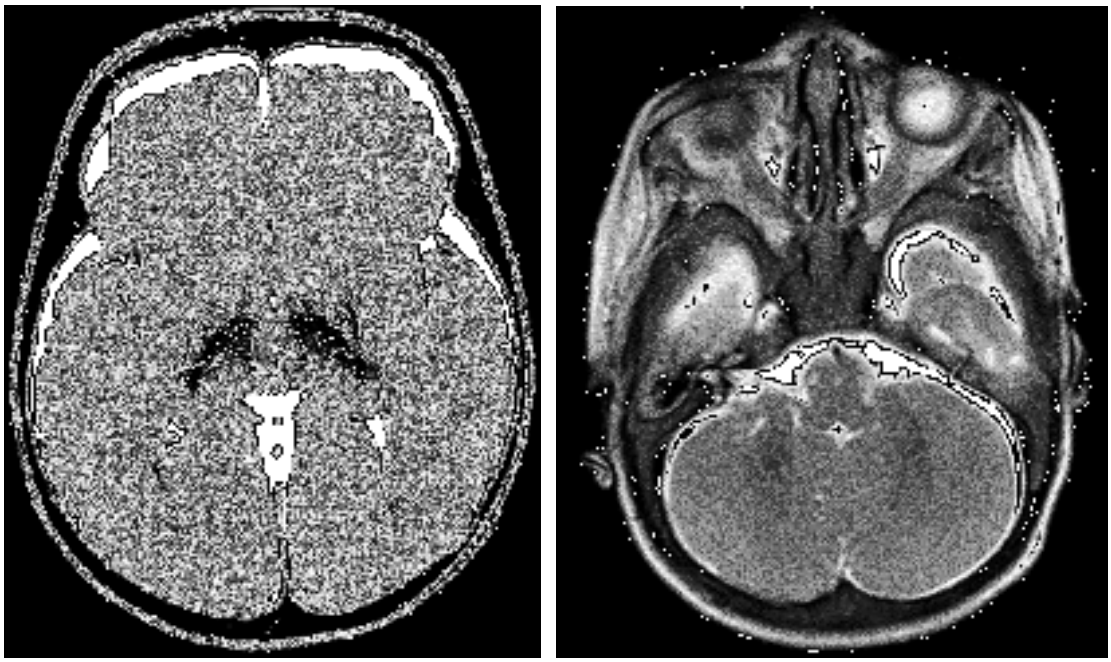
ADC Maps axial

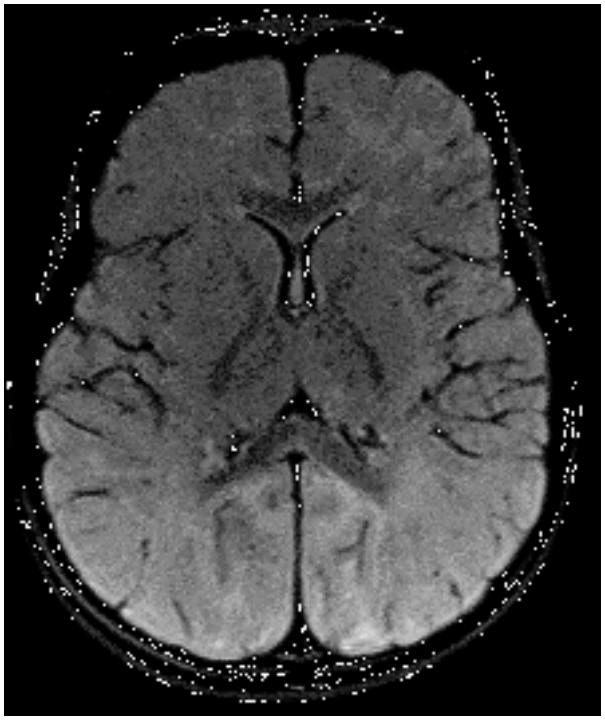
FLAIR sequence axial

Figure 38: Description and radiological images of a case of with Acute Disseminated Encephalitis with bilateral optic neuritis.

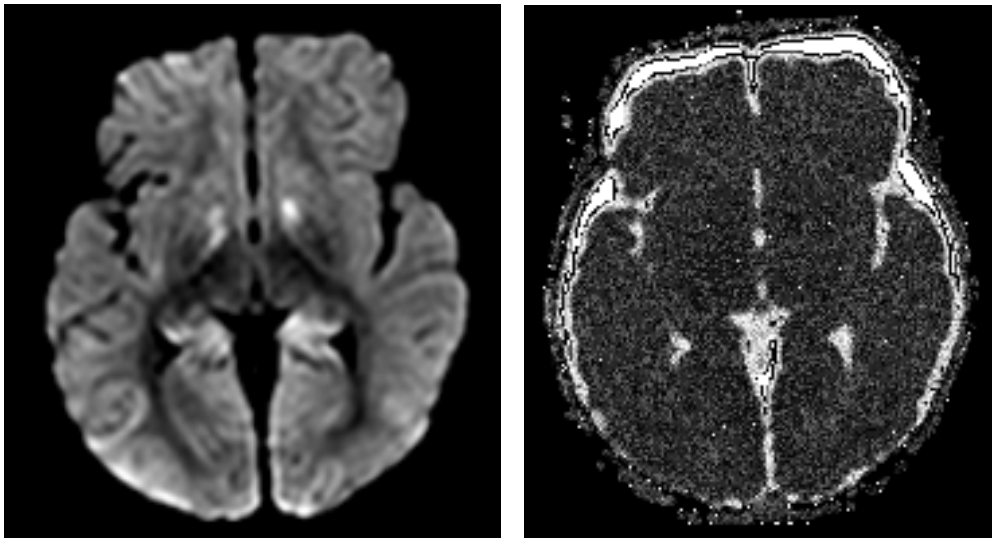
Case 2: A 1-year-old female patient came with a history of difficulty in walking for 5 days with 3 episodes of involuntary jerky movements of all the limbs lasting more than 4 minutes. Her CSF study showed pleocytosis with bihemispheric dysfunction with slow waves on EEG. On MRI, there were Subtle T2 hyperintensities in the retrobulbar portion of the bilateral optic nerves with prominent subarachnoid spaces suggestive of optic neuritis. There were symmetrical T2 and FLAIR hyperintensities in the bilateral posterior parieto- occipital regions with Sub prominent dural spaces predominantly in the bilateral frontal regions. There is evidence of T2 hyperintensities in the bilateral globi pallidi, which show restriction on DWI sequence



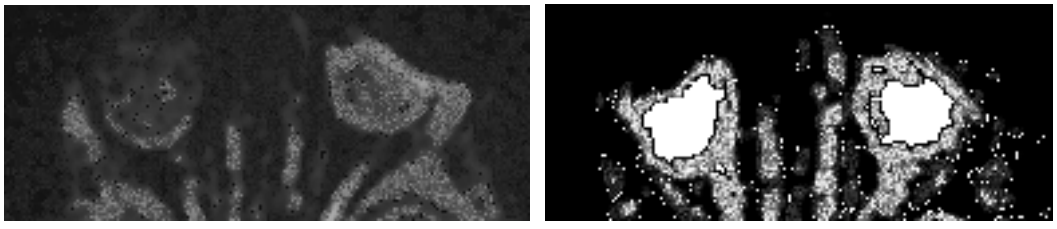
T2 sequence axial



FLAIR sequence axial



DWI sequence with corresponding ADC maps axial

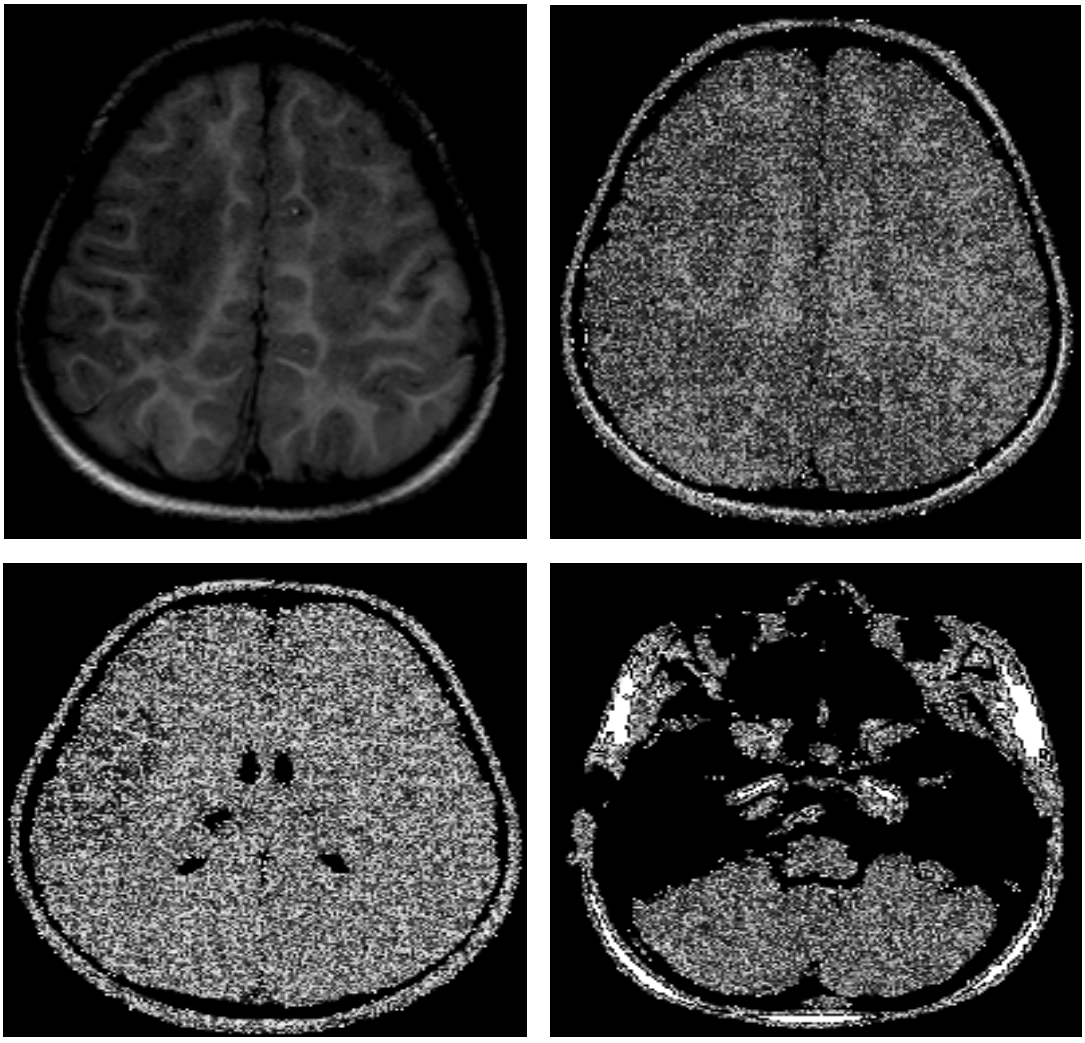


DWI sequence with corresponding ADC map (axial) indicating optic neuritis.

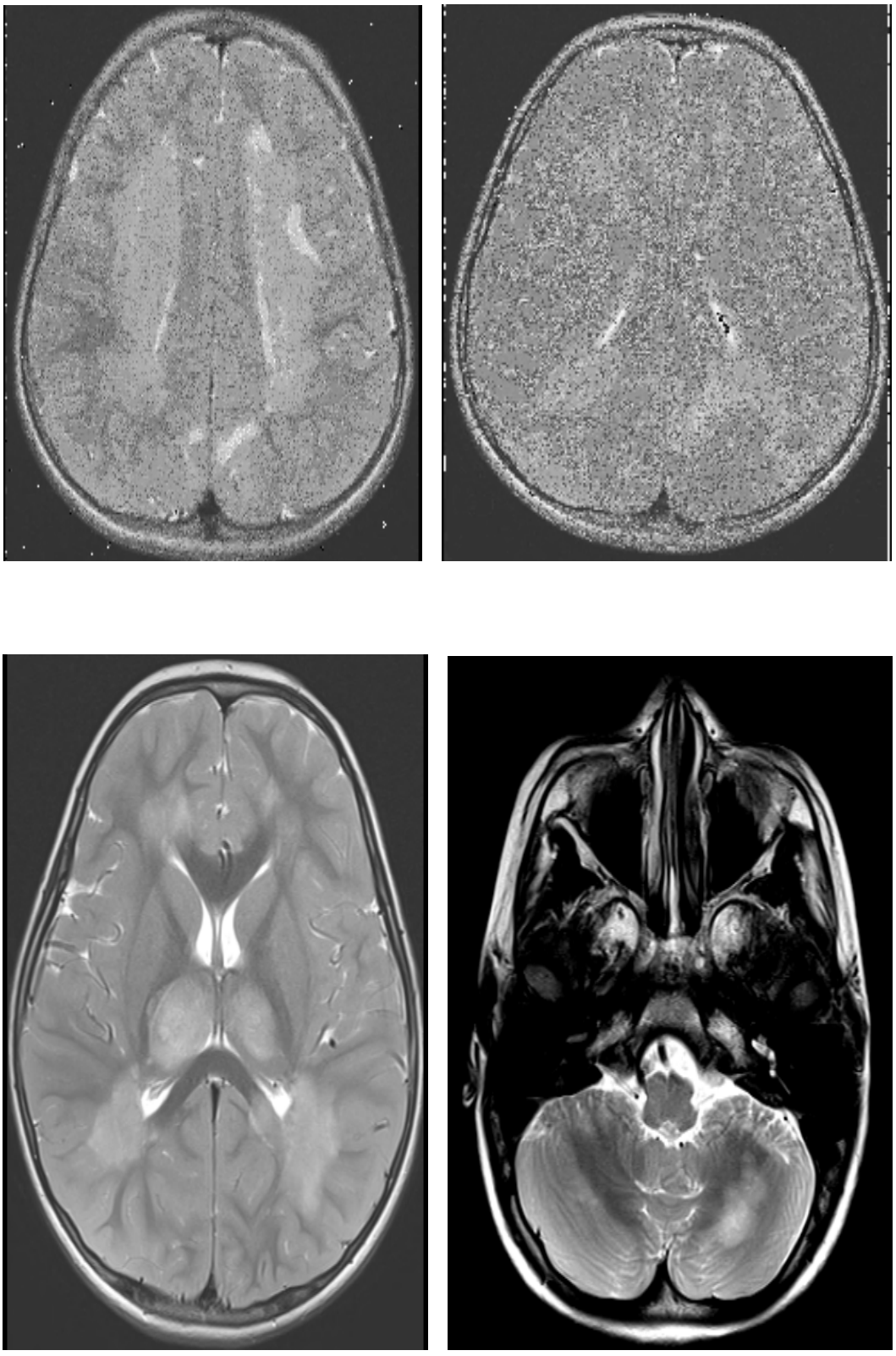
Figure 39: Description and radiological images of a case of with Acute necrotizing encephalitis.

Case 3: A 4-year-old male presented with fever for 6 days with 5 episodes of convulsion with one episode of status epilepticus. CSF analysis did not show pleocytosis, however showed raised proteins. EEG was suggestive of low voltage bi-parietal sharp waves suggestive of epileptiform changes. On MRI, there were symmetric areas of T1 hypointense, T2, and FLAIR hyperintensities involving the bilateral frontoparietal white matter, bilateral centrum semi ovale &corona radiata, bilateral peritrigonal and periventricular regions, left cerebellar lobe, and bilateral thalami.

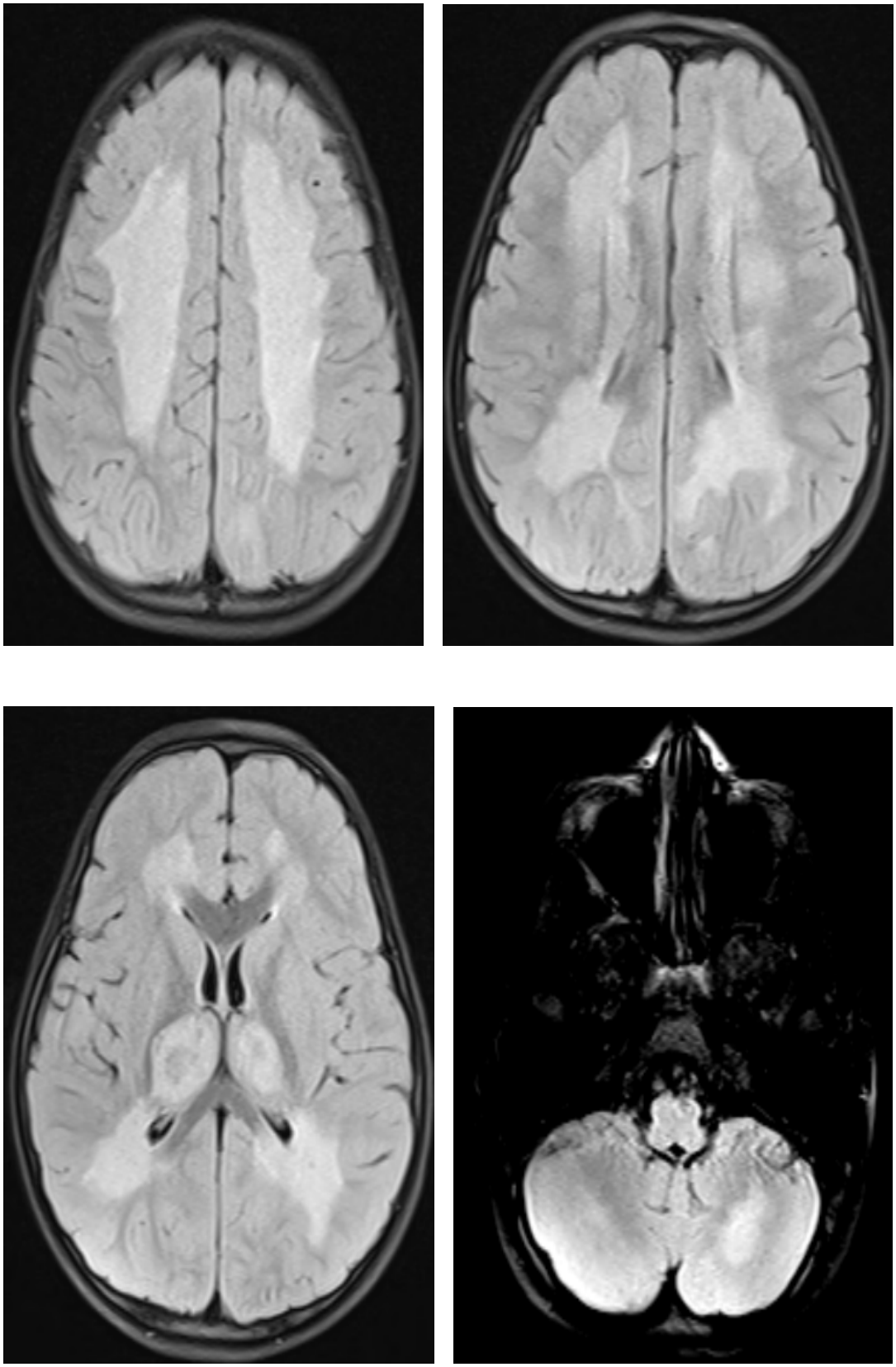
Which showed diffusion restriction on DWI sequence. Areas of blooming were seen involving bilateral thalami and bilateral centrum semi ovale.



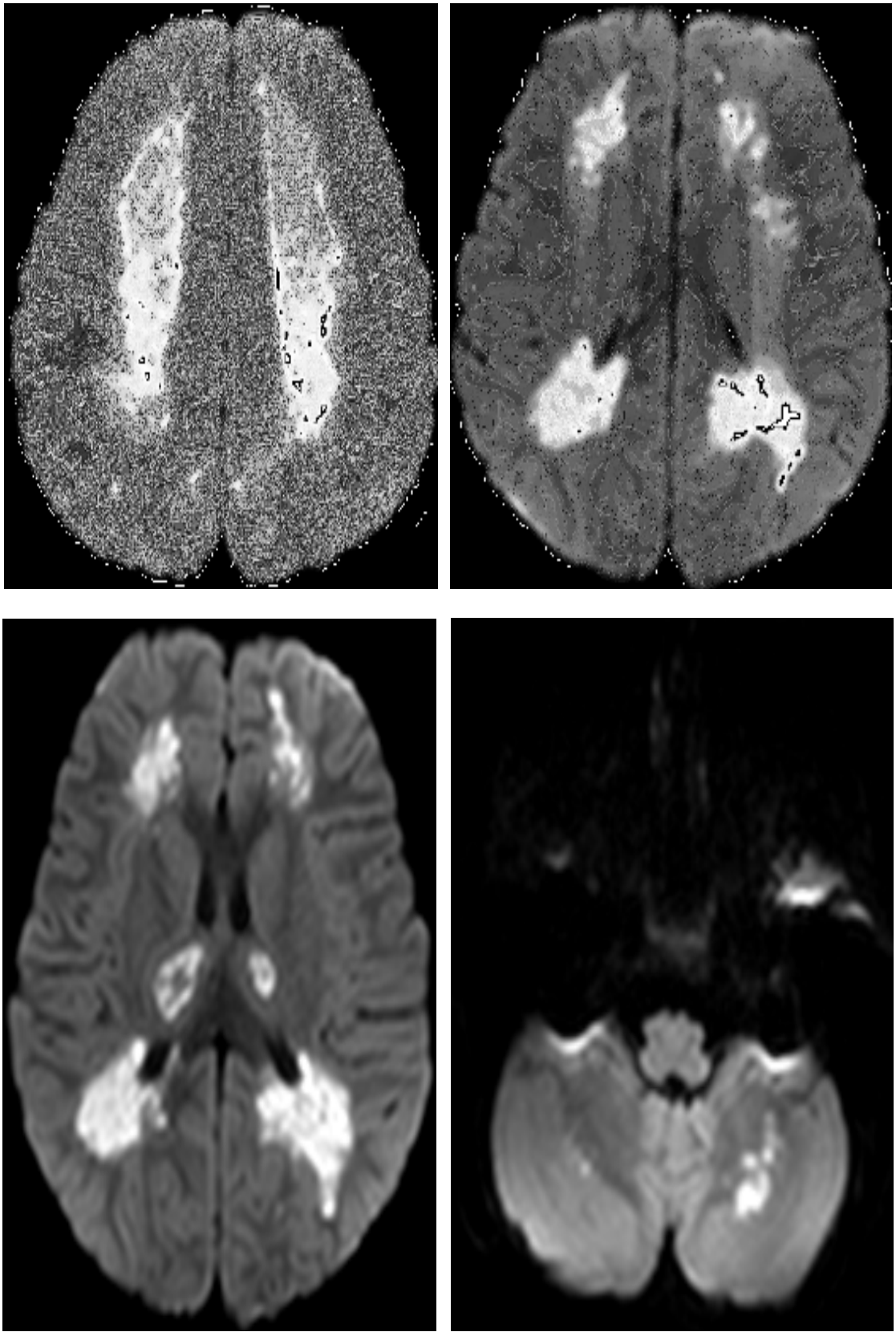
T1 sequence axial



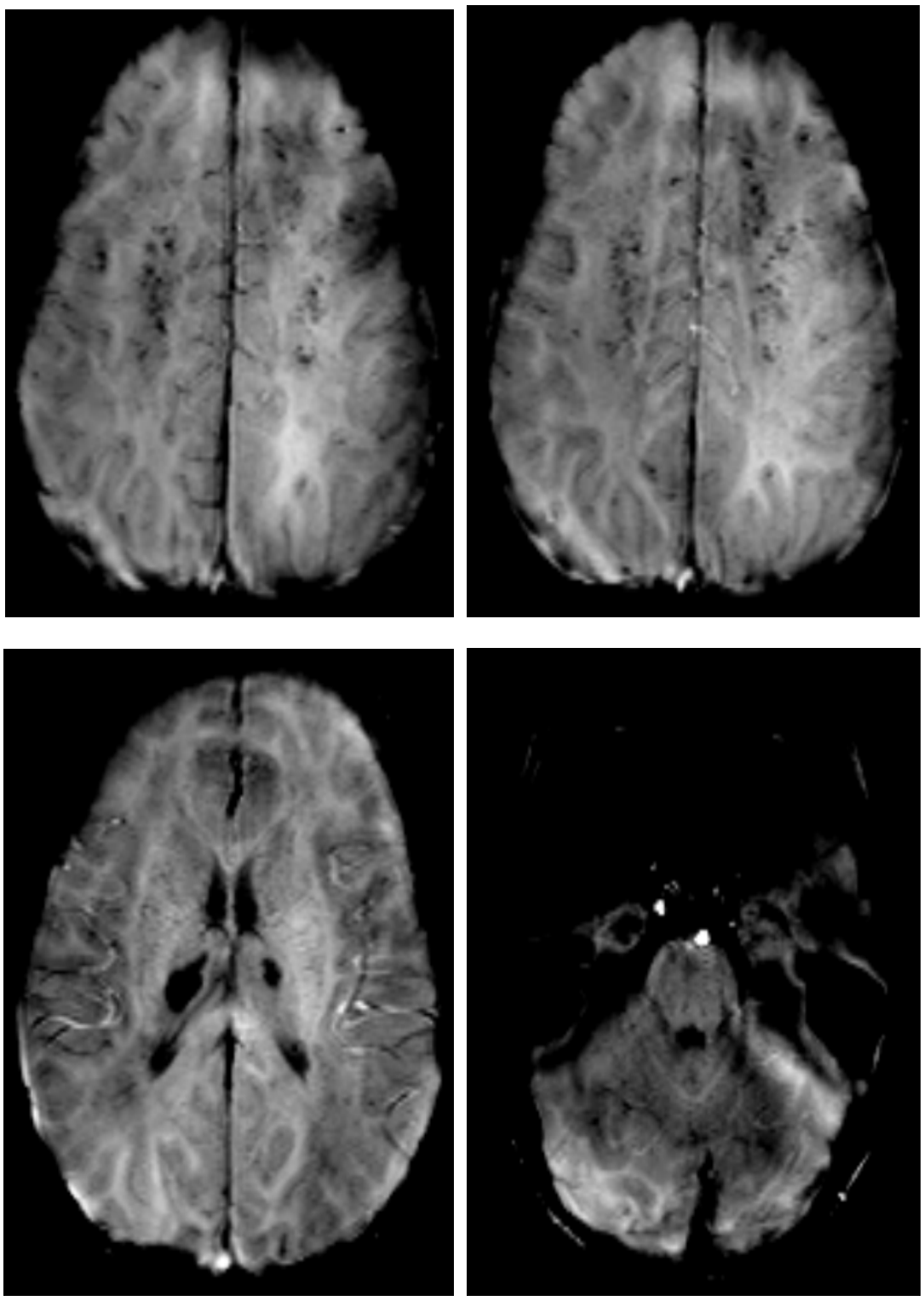
T2 sequence axial



FLAIR Sequence axial



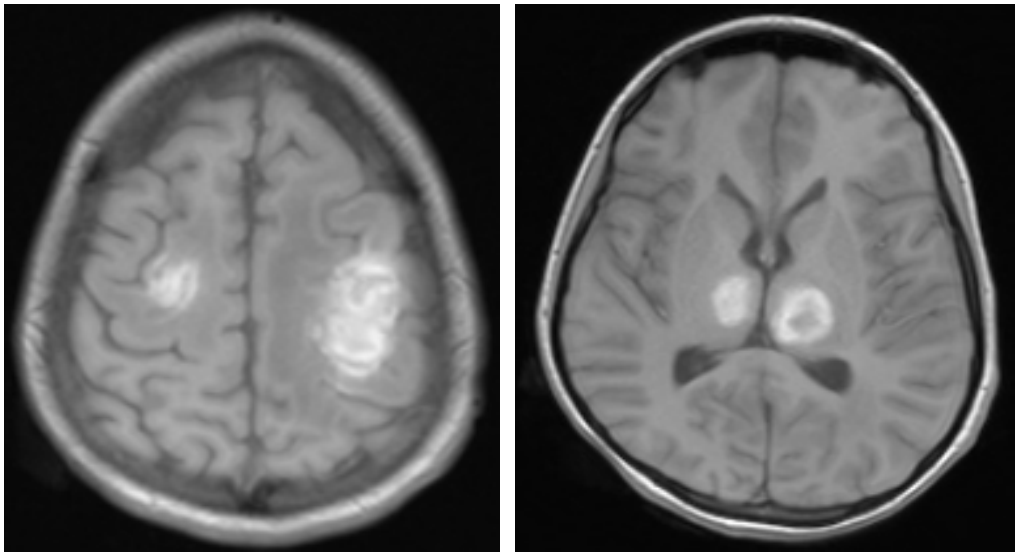
DWI Sequence axial



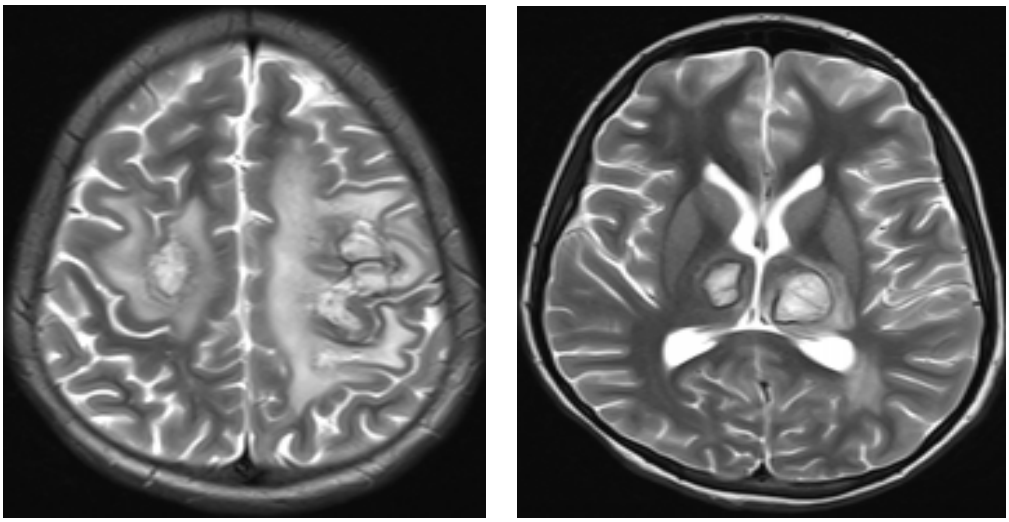
SWI Sequence axial

Figure 40: Description and radiological images of a case of with Dengue haemorrhagic encephalitis.

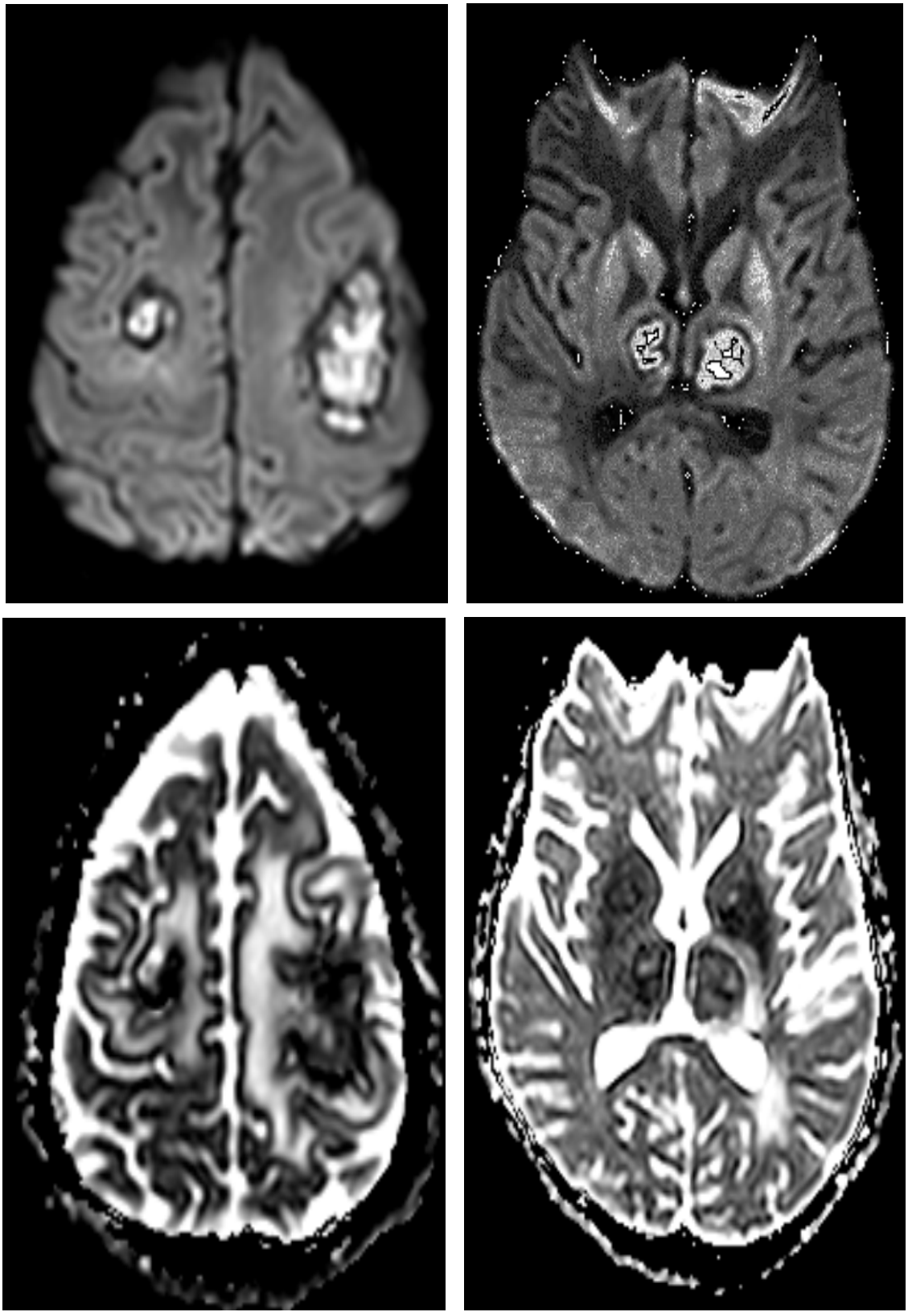
Case 4: A 14-year-old female came with a history of altered sensorium for 12 days, fever with a headache for 8 days, with 3 episodes of convulsions. Her blood serology was positive for NS1 antigen with positive IgM & IgG titres. Her CSF analysis showed raised proteins with pleocytosis. Her EEG was suggestive of right hemispheric dysfunction. On MRI, T1, T2, and FLAIR hyperintense areas with peripheral T2 hypointense rim and significant perilesional edema were seen involving bilateral thalami, cortical & subcortical right frontal & left frontoparietal regions also showing restriction on DWI sequence, and areas of peripheral blooming on SWI sequence. T2 & FLAIR hyperintense and T1 iso-hyperintense areas with areas of blooming on SWI sequence were seen in the right frontal, right temporal, left parietal, and left cerebellar lobe.



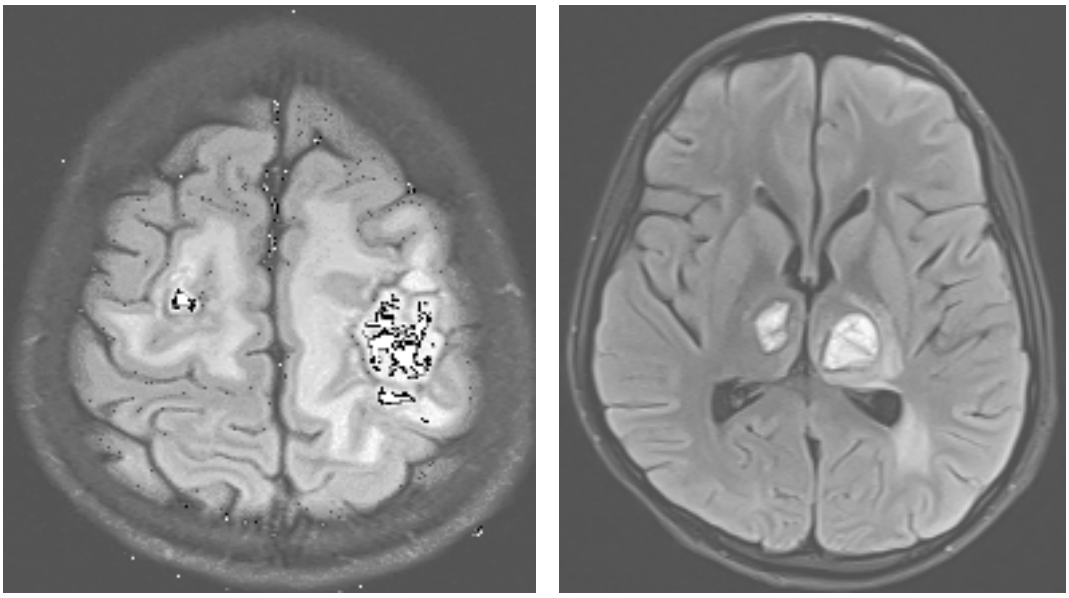
T1 sequence axial



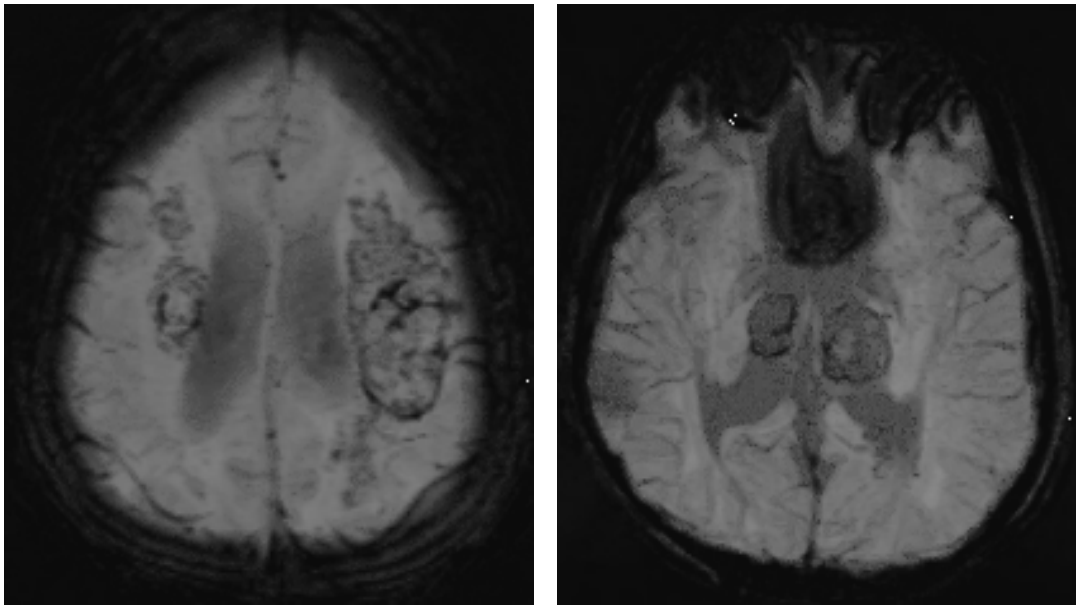
T2 Sequence axial



DWI Sequence with corresponding ADC maps (axial).



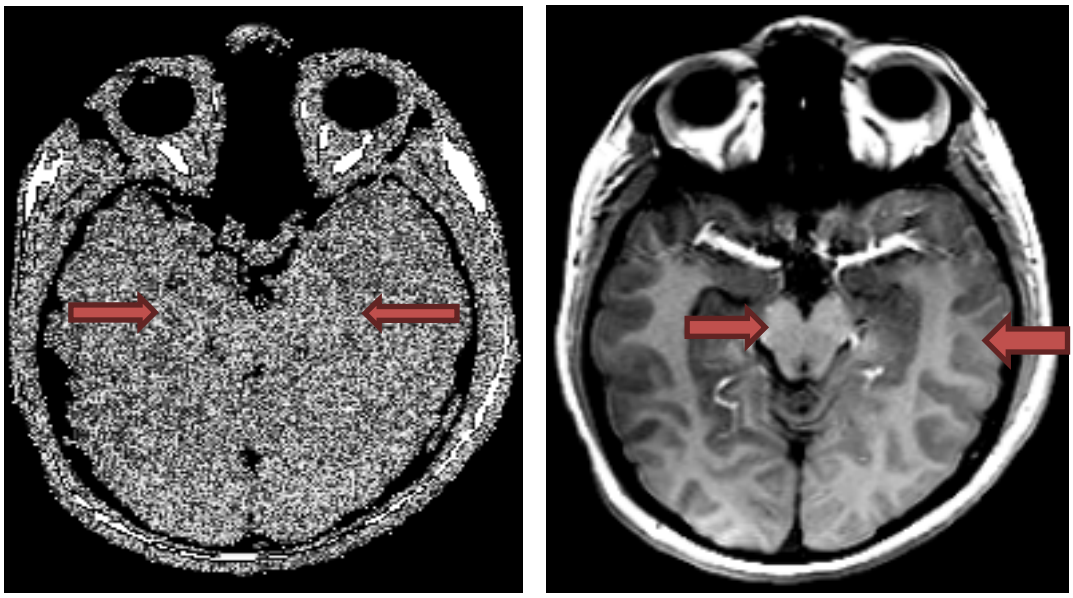
FLAIR Sequence axial



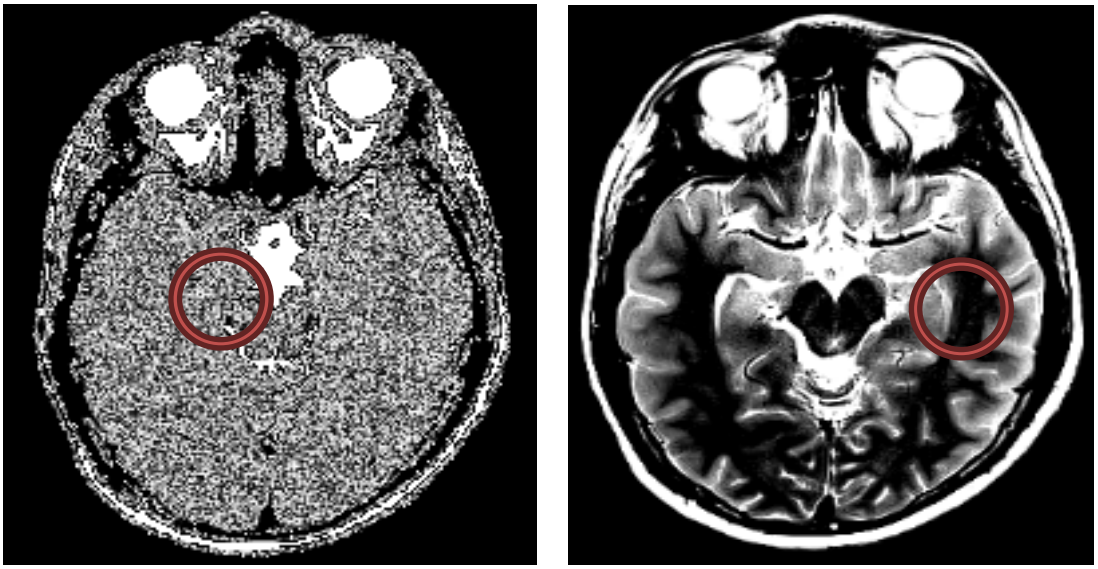
SWI Swquence axial

Figure 41: Description and radiological images of a case of with herpes simplex encephalitis.

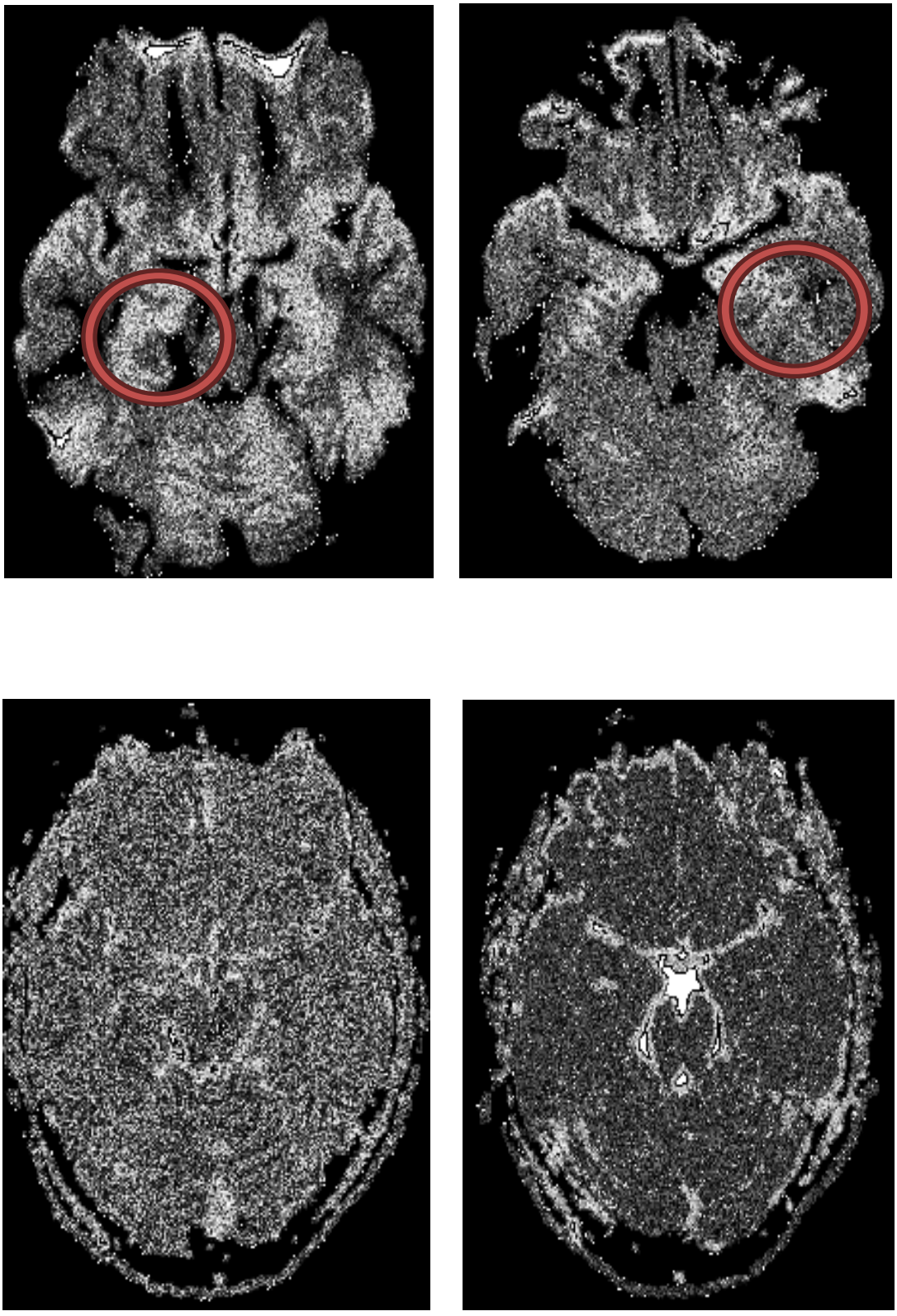
Case 5: 17-year-old male presented with a history of fever for 6 days with 2 episodes of convulsion, delusional and aggressive behaviour. The CSF analysis shows pleocytosis with raised protein levels. EEG showed abnormal periodic discharges involving both the cerebral hemispheres. On MRI, there were symmetrical T1 hypointense, T2 & FLAIR hyperintense areas in the bilateral uncal and medial temporal region with areas of restriction on DWI sequence. No areas of blooming were seen on the SWI sequence.



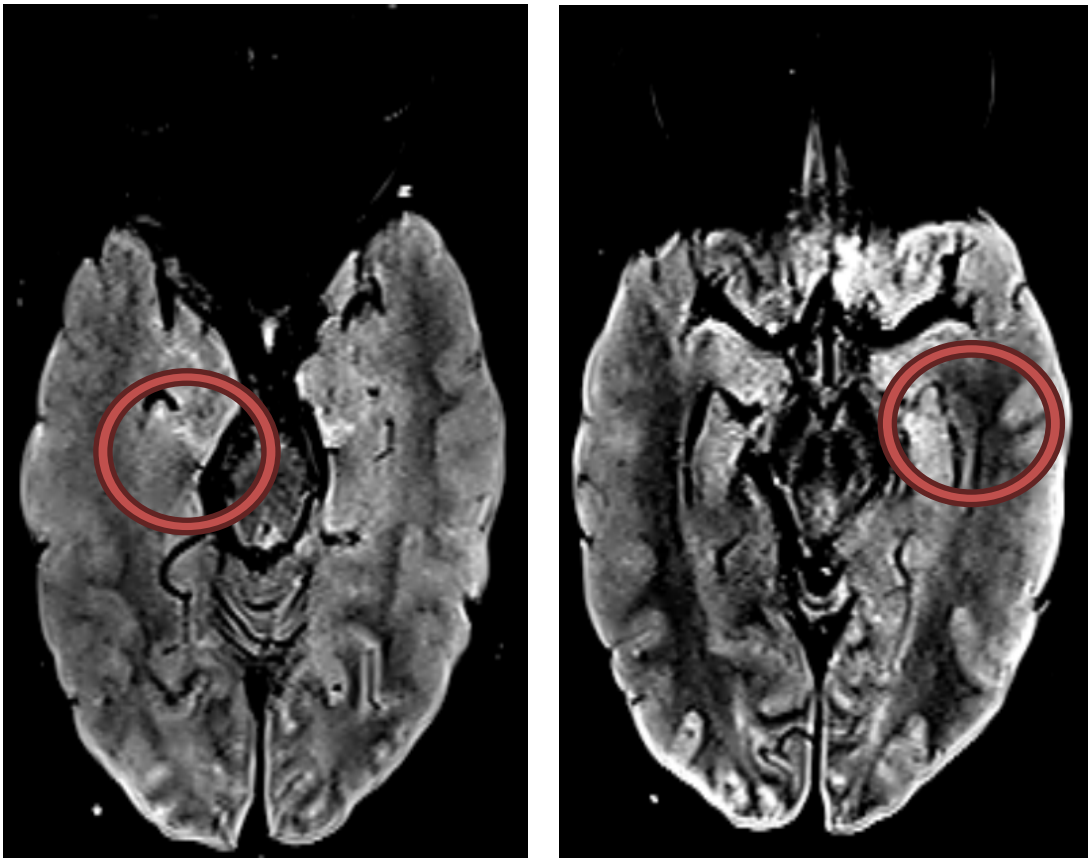
T1 Sequence axial



T2 Sequence axial



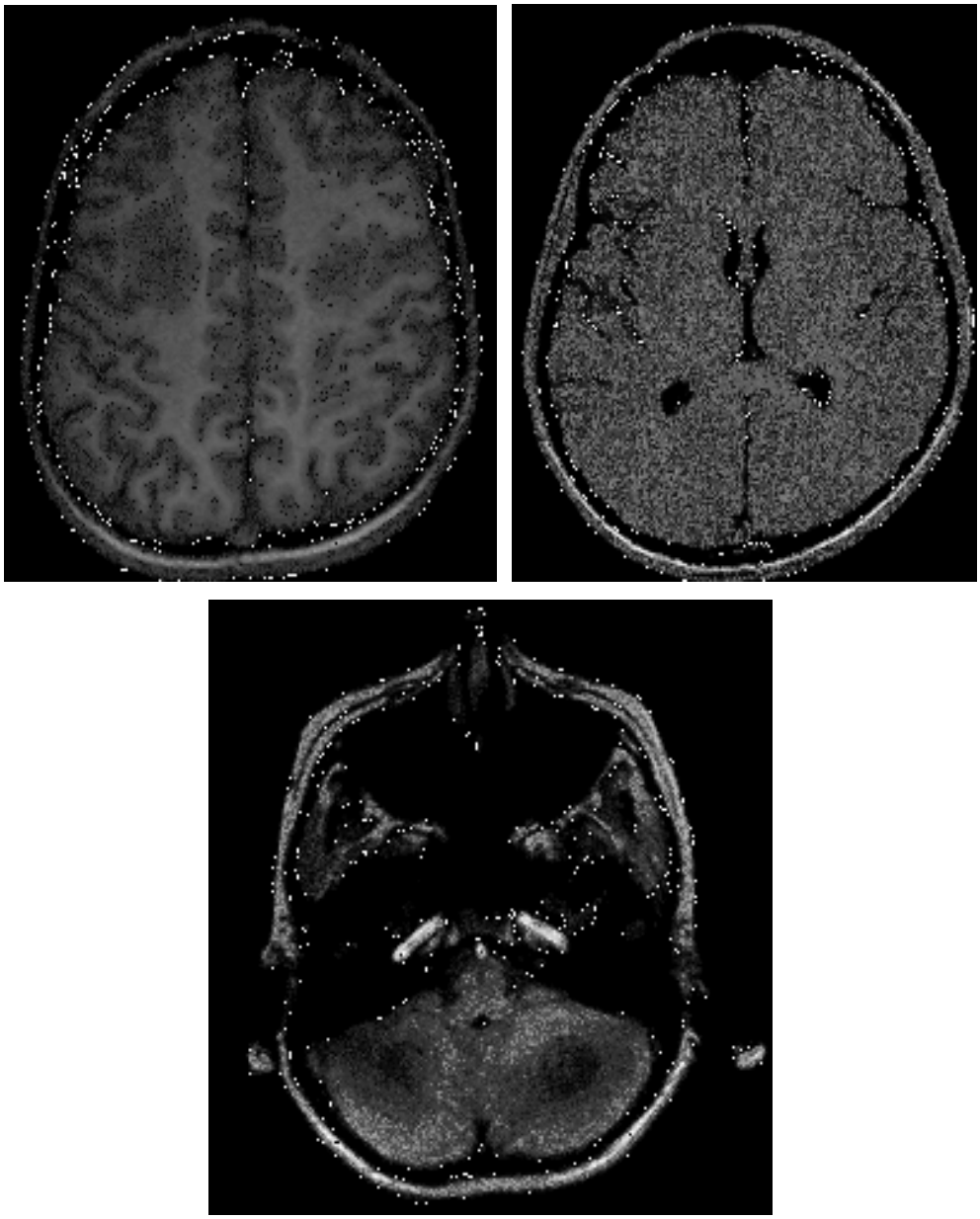
DWI Sequence with diffusion restriction and corresponding ADC maps (axial).



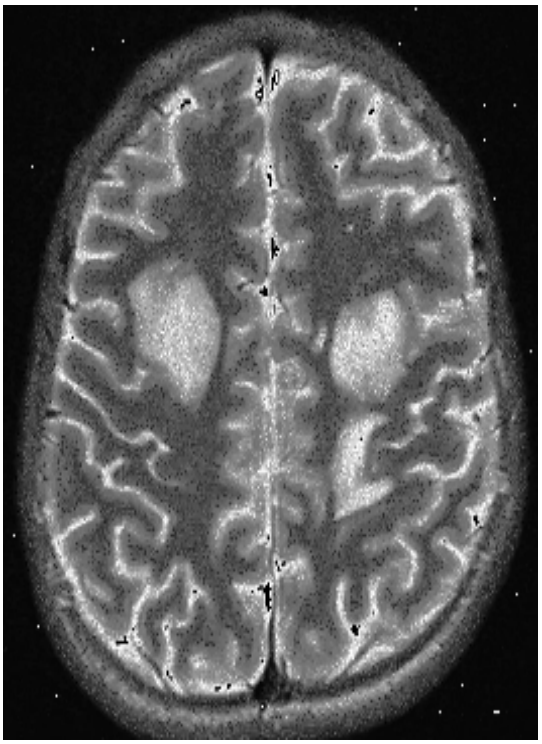
FLAIR Sequence axial

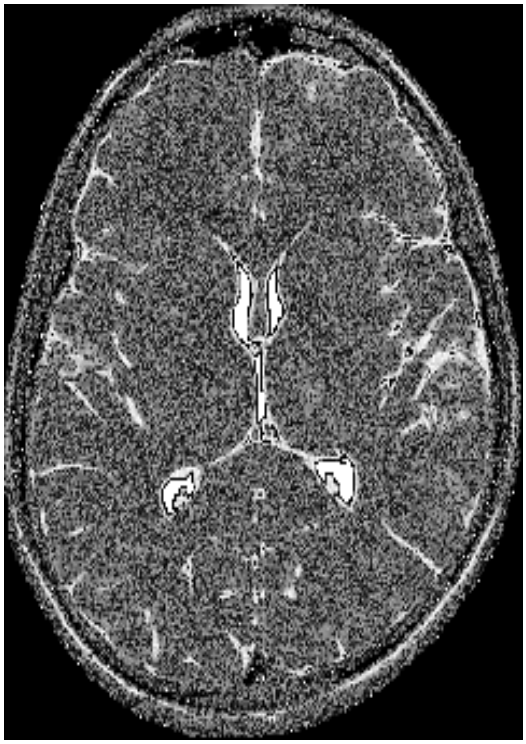
Figure 42: Description and radiological images of a case of with acute haemorrhagic leukoencephalitis.

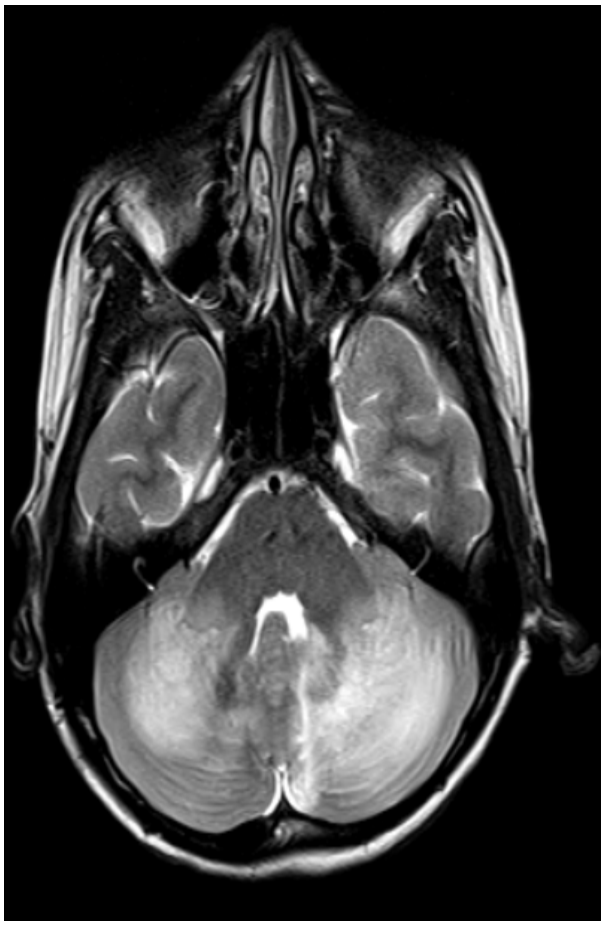
Case 6: A 13-year-old male presented with a history of fever for 6 days with and right upper and lower limb weakness, ataxia, and aggressive behaviour. His CSF analysis showed raised protein levels, xanthochromia, RBCs with pleocytosis. EEG showed low voltage bi-parietal sharp waves suggestive of epileptiform activity. On MRI Brain examination, there were seen T2 & FLAIR hyperintense and T1 hypointense areas involving bilateral frontal & parietal subcortical white matter, left thalamus, right peritrigonal region, and bilateral cerebellar lobes & vermis with areas of diffusion restriction on DWI sequence. Few areas of blooming were seen on the SWI sequence in the left cerebellar lobe and left peri-rolandic region suggestive of hemorrhage.



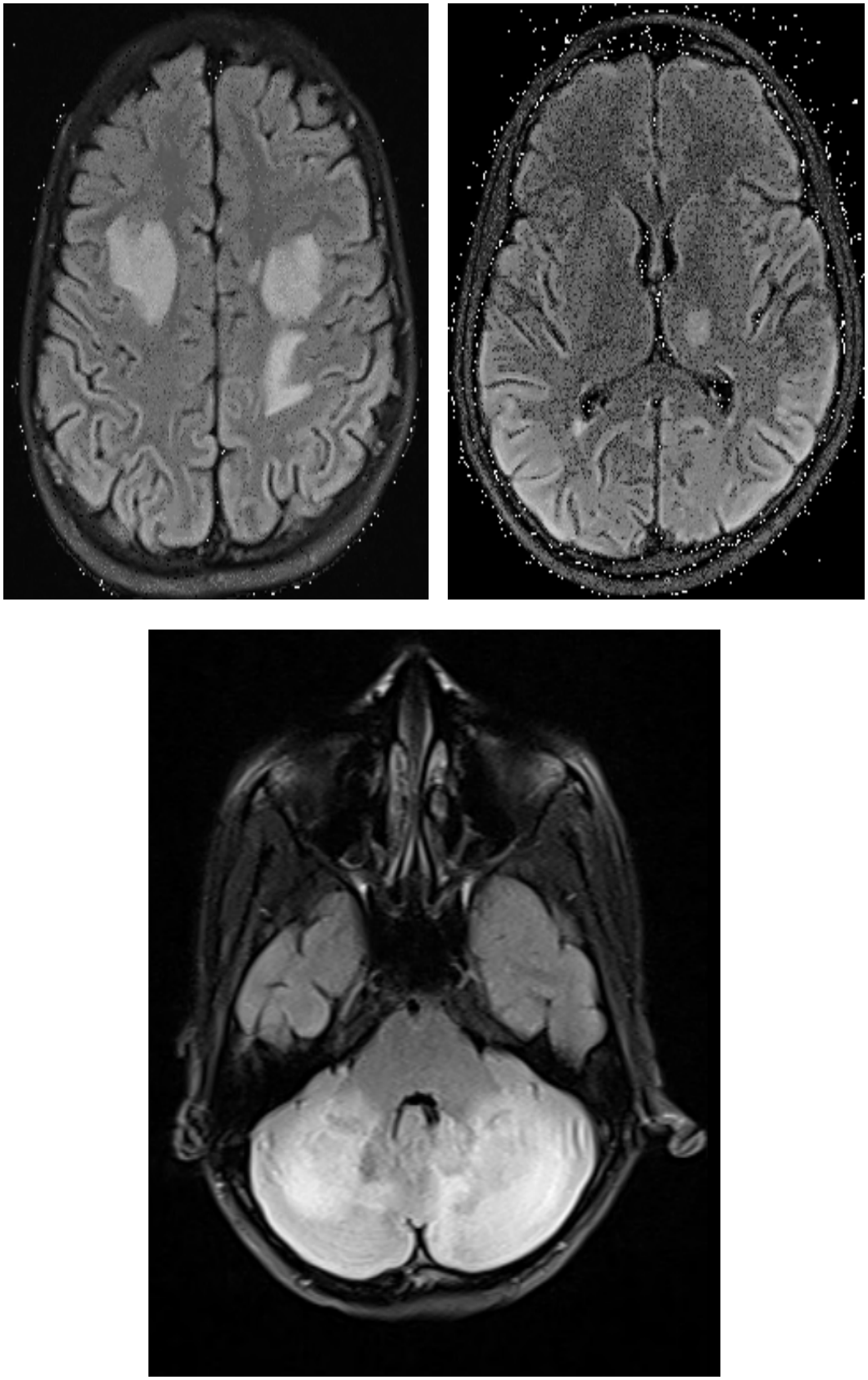
T1 Sequence axial



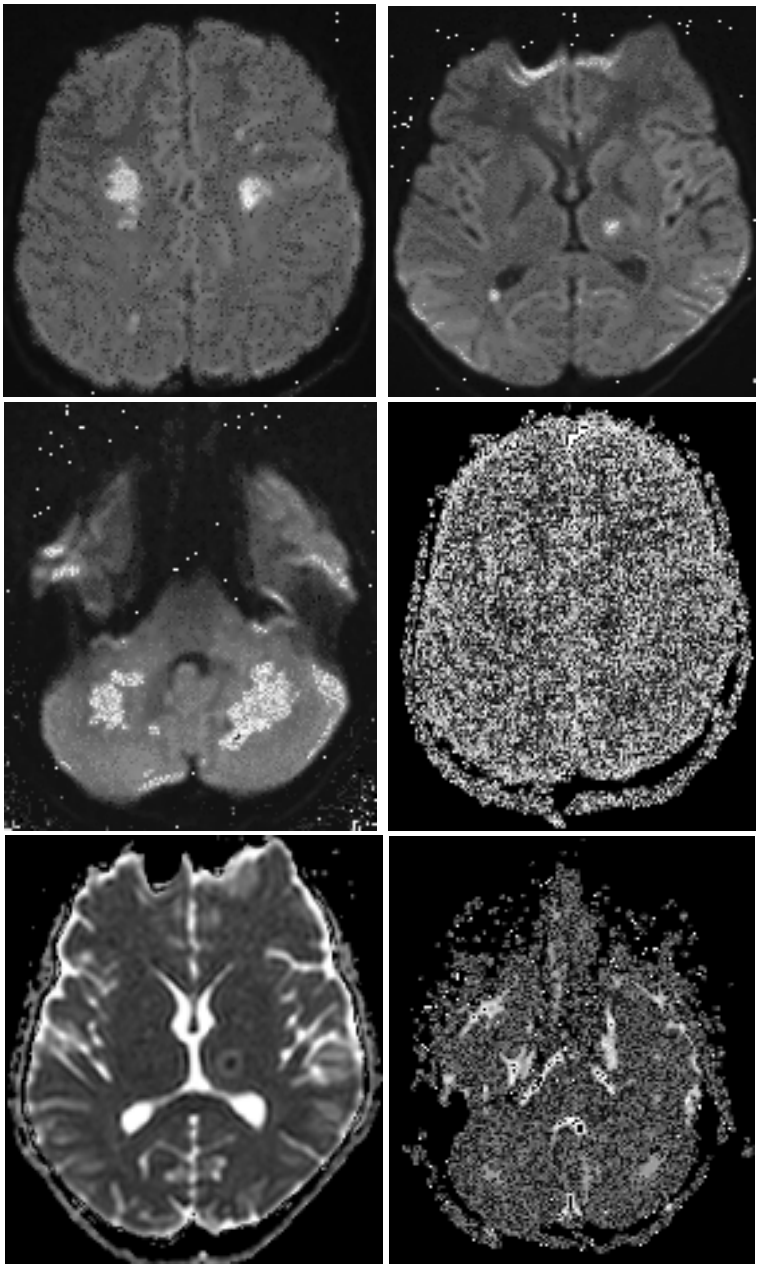




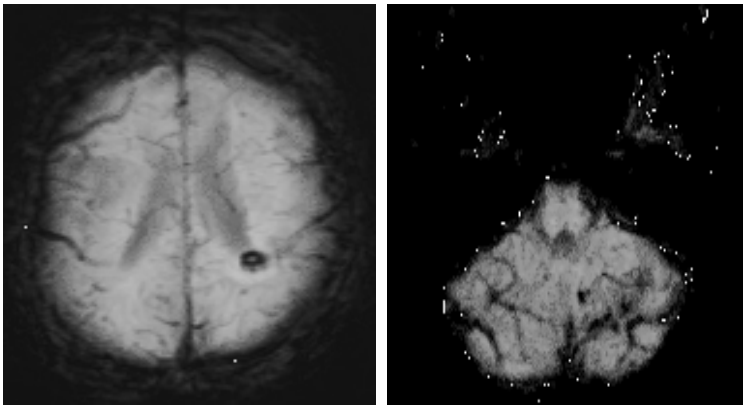
T2 sequence axial



FLAIR Sequence axial



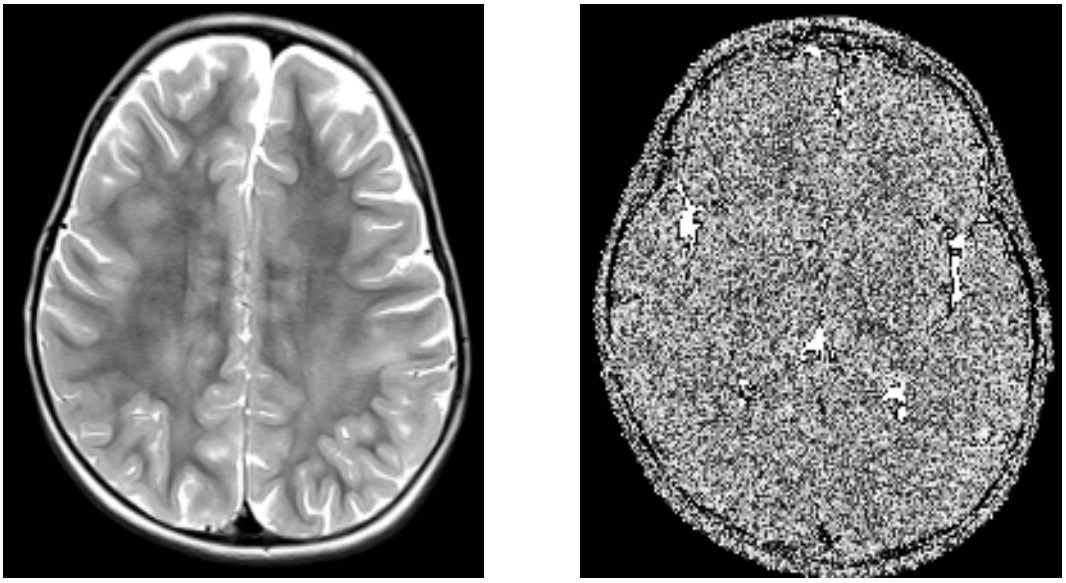
DWI Sequence with corresponding ADC maps (axial).



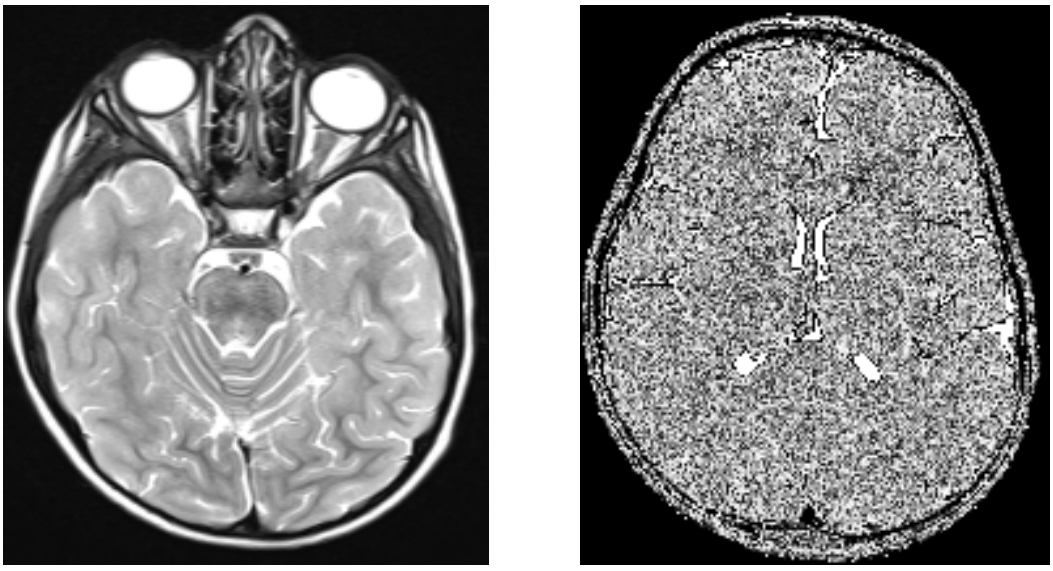
SWI sequence axial.

Figure 43: Description and radiological images of a case of with acute disseminated encephalomyelitis.

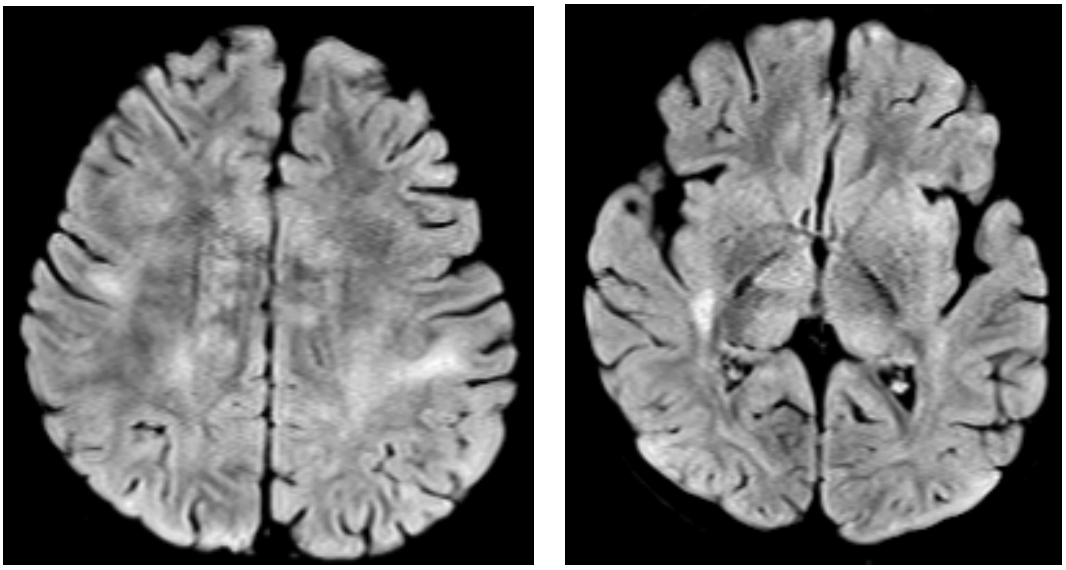
Case 7: A 3-year-old male came with fever for 10 days with 4 episodes of convulsions and stiffness of all the limbs for 2 days. The EEG showed occasional sharp and slow-wave discharges over bilateral centroparietal leads; however, the anti-MOG antibody was negative, and the CSF analysis was within normal limits. On MRI Brain, bilateral asymmetric T2 & FLAIR hyperintensities were seen involving the fronto-parieto-temporo-occipital subcortical white matter, centrum semiovale, thalami, pons, bilateral middle cerebellar peduncles, cerebellar white matter, and entire corpus callosum. Subtle T2 hyperintensities were noted involving bilateral basal ganglia and medulla.



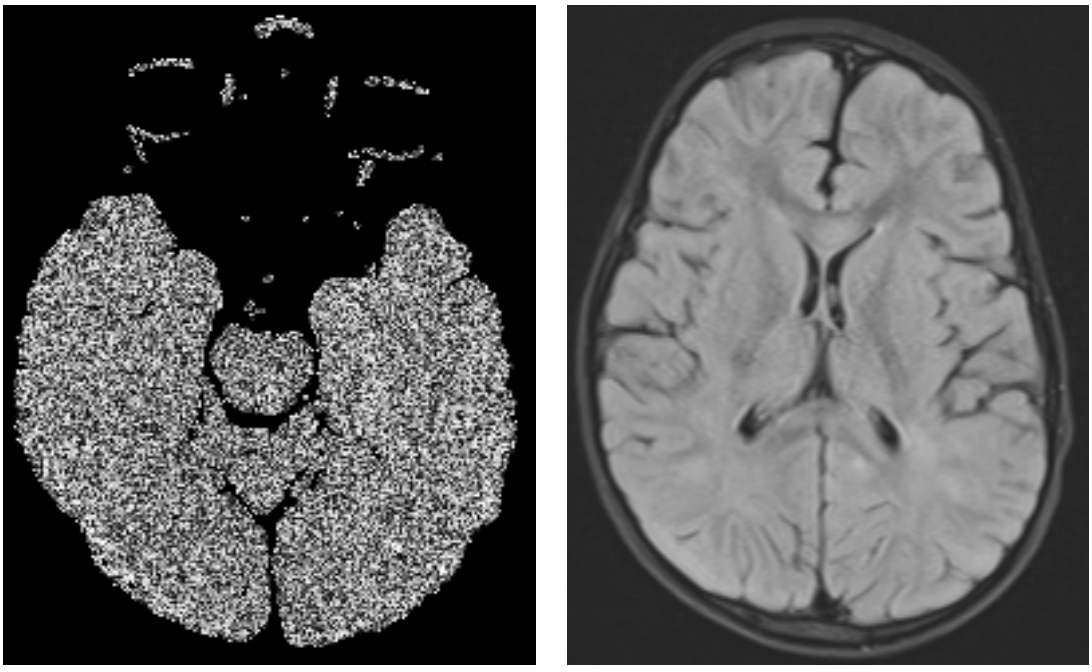
T2 Sequence axial



T2 sequence axial



FLAIR Sequence axial.



FLAIR Sequence axial.

ANNEXURE V- KEY TO MASTER CHART

Variable	Key
Sex	1=Male, 3=Female
Developmental history	0=normal,1=abnormal
Past history	0=nothing significant, 1=history of respiratory tract infections, 2=history of gastro, 3=history of dengue fever.
Anatomical locations (occipital lobe to temporal lobe)	0=Normal, 1= Positive for AES
T1	0=Isointense, 1=Hypointense
T2	=Isointense, 1=Hyperintense
FLAIR	0=Isointense, 1=Hyperintense
DWI	0=No restricted diffusion, 1=restricted diffusion
SWI	0=No blooming, 1=blooming
ADC	0=No Reversal on ADC Maps, 1= Reversal on ADC maps
MRS	0=Normal, 1= abnormal

ANNEXURE VI- MASTER SHEET

SL NO.	Age (years)	Sex	Birth history	Chief complaints	Developmental history	Immunization history	Past history	Provisional diagnosis	Occipital lobe	Centrum semi vale	Corona radiata	Corpus callosum	Caudate nucleus	Caudate nucleus	Lentiform nucleus	Subthalamic nucleus	Substantia nigra	Cerebellar hemispheres	Median vermis	Thalamus	Tectum	Tegmentum	Cerebral peduncles
1	10	1	NICU admission	Limb weakness and stiffness	0	Up to date	1	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	2	2	Normal	convulsions, limb problem	0	Not up to d	1	Acute encephalitis syndrome	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
3	1	2	Normal	altered sensorium, fever	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	1	2	NICU admission	Limb weakness and stiffness	0	Up to date	2	Acute encephalitis syndrome	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0
5	4	1	Normal	fever, convulsions	0	Up to date	0	Acute encephalitis syndrome	0	1	1	0	0	0	0	0	0	1	1	1	0	0	0
6	16	1	Normal	altered sensorium, fever	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	1	2	Normal	fever, convulsions	0	Not up to d	0	Acute encephalitis syndrome	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0
8	1	2	NICU admission	Limb weakness, fever	0	Up to date	0	Acute encephalitis syndrome	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0
9	17	1	Normal	fever, convulsions, delusion	0	Up to date	1	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	14	2	Normal	altered sensorium, fever, headache	0	Up to date	3	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0
11	18	2	Normal	convulsions, limb stiffens, fever	0	Up to date	3	Acute encephalitis syndrome	0	1	1	1	1	1	1	0	0	1	0	1	0	0	0
12	18	1	Normal	Fever	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	1	2	Normal	fever, convulsions	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	5	2	NICU admission	Limb weakness and stiffness	0	Not up to d	1	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15	5	1	Normal	altered sensorium, limb weakness	0	Not up to d	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
16	1	2	Normal	fever, convulsions	0	Up to date	2	Acute encephalitis syndrome	0	0	0	0	1	1	1	0	0	0	0	1	0	1	0
17	13	1	Normal	aggression, fever, limb weakness	0	Not up to d	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0
18	2	1	Normal	Limb weakness and stiffness	0	Up to date	1	Acute encephalitis syndrome	0	0	0	0	1	1	1	0	0	0	0	1	1	1	0
19	2.5	1	NICU admission	fever, convulsions, seizures	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	1	2	NICU admission	fever, limb stiffness, decreased awareness	0	Not up to d	0	Acute encephalitis syndrome	1	1	1	0	1	1	1	0	0	0	0	0	0	0	0
21	10	2	Normal	headache, vomiting, fever	0	Up to date	1	Acute encephalitis syndrome	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
22	3	1	Normal	fever, convulsions, limb weakness	0	Up to date	1	Acute encephalitis syndrome	1	1	0	1	1	1	1	0	0	0	0	1	0	0	0
23	8	1	Normal	fever, convulsions, limb weakness	0	Up to date	0	Acute encephalitis syndrome	1	0	0	0	1	1	1	0	0	0	0	1	0	0	0
24	17	1	Normal	altered sensorium, fever	0	Not up to d	0	Acute encephalitis syndrome	1	0	0	0	1	1	1	0	0	0	0	0	0	0	1
25	12	1	Normal	Limb weakness and stiffness, fever	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
26	18	1	Normal	Limb weakness and stiffness, fever	0	Up to date	1	Acute encephalitis syndrome	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
27	18	2	Normal	fever, delusion	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
28	17	2	Normal	fever, altered sensorium	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
29	9	1	Normal	fever, convulsions, delusion	0	Up to date	2	Acute encephalitis syndrome	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	16	2	Normal	fever, convulsion, Limb weakness and stiffness	0	Not up to d	3	Acute encephalitis syndrome	0	0	0	0	1	1	1	0	0	0	0	1	0	0	0
31	9	1	Normal	fever, convulsion, Limb weakness and stiffness	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0
32	18	1	Normal	fever, convulsions, depression, limb weakness	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
33	1	1	NICU admission	fever, limb weakness	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

34	1	2	Normal	fever, limb weakness	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
35	3	1	NICU admission	fever, convulsions	0	Up to date	2	Acute encephalitis syndrome	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
36	9	1	Normal	fever, altered sensorium	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
37	13	1	Normal	fever, limb problem	0	Up to date	0	Acute encephalitis syndrome	0	1	1	1	0	0	0	0	0	1	0	0	0	1	0
38	11	1	Normal	fever, convulsions, depression	0	Not up to d	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
39	2	1	NICU admission	fever, convulsions	0	Not upto da	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
40	17	1	Normal	fever, headache	0	Not upto da	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
41	3	2	Normal	fever, vomit, altered sensorium	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
42	13	2	Normal	fever, limb problem	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
43	11	2	Normal	fever, convulsions	0	Not up to d	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
44	11	1	Normal	fever, convulsions, aggression	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
45	7	1	Normal	fever, convulsions	0	Up to date	1	Acute encephalitis syndrome	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
46	5	1	NICU admission	Limb weakness and stiffness	0	Up to date	0	Acute encephalitis syndrome	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
47	9	2	Lscs	fever, vomit, blurred vision	0	Up to date	1	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
48	13	2	Normal	headache, convulsions	1	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
49	4	1	NICU admission	Limb weakness and stiffness	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50	2	1	Normal	fever, altered sensorium	0	Up to date	1	Acute encephalitis syndrome	0	1	1	0	0	0	1	0	0	1	0	1	0	0	0
51	7	1	Normal	fever, vomit, altered sensorium	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
52	10	2	Normal	fever, vomit, altered sensorium	0	Up to date	0	Acute encephalitis syndrome	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
53	1	2	Normal	altered sensorium, convulsions, fever	0	Up to date	1	Acute encephalitis syndrome	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
54	13	1	Normal	fever, vomit, altered sensorium	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
55	7	1	Normal	fever, headache	0	Up to date	1	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
56	16	2	Normal	fever, seizures	0	Up to date	0	Acute encephalitis syndrome	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
57	18	1	Normal	fever, headache	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
58	4	1	Normal	fever, limb problem	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
59	1.5	1	NICU admission	fever, drowsiness	0	Up to date	1	Acute encephalitis syndrome	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0
60	10	2	Normal	fever, convulsions, memory loss	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
61	12	1	Normal	fever	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
62	6	1	NICU admission	altered sensorium, convulsions	0	Up to date	1	Acute encephalitis syndrome	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
63	1	1	Normal	fever	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
64	1	1	NICU admission	fever	0	Up to date	2	Acute encephalitis syndrome	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
65	11	1	Normal	fever, headache	0	Up to date	1	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
66	16	1	Normal	fever, convulsion	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
67	6	1	Normal	fever, headache, convulsion	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
68	14	1	Normal	fever, ache	0	Up to date	0	Acute encephalitis syndrome	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

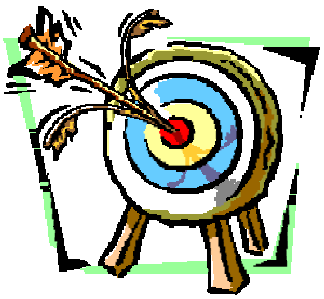
SL NO.	Corpora quadrigemina	Posterior perforated substance	Periaqueductal grey	Internal capsule	Cerebellar peduncles	Pons	Medulla oblongata	Frontal lobe	Parietal lobe	Temporal lobe	RADIOLOGICAL DIAGNOSIS	RADIOLOGICAL DIAGNOSIS
1	0	0	0	0	0	0	0	1	1	1	Para infectious	ACUTE DISSEMINAYED ENCEPHALOMYELITIS
2	0	0	0	1	0	0	0	0	0	0	Non-infectious	RASMUSSENS ENCEPHALITIS
3	0	0	0	0	0	0	0	0	0	1	Infectious	VIRAL ENCEPHALITIS
4	0	0	0	0	0	0	0	0	1	0	Para infectious	ACUTE DISSEMINAYED ENCEPHALOMYELITIS WITH BILATERAL OPTIC NEURITIS
5	0	0	0	0	0	0	0	1	1	0	Para infectious	ACUTE NECROTIZING ENCEPHALITIS
6	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
7	0	0	0	0	1	0	0	1	1	1	Para infectious	ENCEPHALITIS WITH INTRAPARENCHYMAL BLEED
8	0	0	0	1	0	1	1	0	0	0	Infectious	VIRAL ENCEPHALITIS
9	0	0	0	0	0	0	0	0	0	1	Non-infectious	AUTOIMMUNE/HSV ENCEPHALITIS
10	0	0	0	0	0	0	0	1	1	1	Para infectious	DENGUE HEMORRHAGIC ENCEPHALITIS
11	0	0	0	0	0	0	0	1	1	1	Para infectious	DENGUE ENCEPHALITIS
12	0	0	0	0	0	1	0	0	0	1	Non-infectious	AUTOIMMUNE ENCEPHALITIS
13	0	0	0	0	0	0	0	1	0	0	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
14	0	0	0	0	0	0	0	1	1	0	Para infectious	ACUTE DISSEMINAYED ENCEPHALOMYELITIS
15	0	0	0	0	0	0	0	0	0	1	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
16	0	0	0	0	0	1	0	1	1	1	Para infectious	ACUTE NECROTIZING ENCEPHALITIS
17	0	0	0	0	0	0	0	1	1	0	Para infectious	ACUTE HEMORRHAGIC LEUKOENCEPHALITIS
18	0	0	0	0	0	0	0	1	1	1	Para infectious	ACUTE HEMORRHAGIC ENCEPHALITIS / ACUTE NECROTIZING ENCEPHALITIS
19	0	0	0	0	0	0	0	0	0	1	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
20	0	0	0	0	0	0	0	1	1	1	Para infectious	HEMORRHAGIC ENCEPHALITIS
21	0	0	0	0	0	1	1	0	1	0	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
22	0	0	0	0	1	1	1	1	1	1	Para infectious	ACUTE DISSEMINAYED ENCEPHALOMYELITIS
23	0	0	0	0	0	0	0	1	1	1	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
24	0	0	0	0	0	0	0	0	0	0	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY WITH VENTRICULITIS
25	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
26	0	0	0	0	0	0	0	1	1	0	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
27	0	0	0	0	0	0	0	0	0	1	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
28	0	0	0	0	0	0	0	1	0	1	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
29	0	0	0	0	0	0	0	0	1	0	Non-infectious	AUTOIMMUNE ENCEPHALITIS

30	0	0	0	0	0	0	0	0	1	1	Para infectious	DENGUE ENCEPHALITIS
31	0	0	0	0	0	0	0	0	0	1	Infectious	JAPANESE ENCEPHALITIS
32	0	0	0	1	0	0	0	0	0	1	Infectious	HSV ENCEPHALITIS
33	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
34	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
35	0	0	0	0	0	0	0	1	0	0	Para infectious	ACUTE DISSEMINAYED ENCEPHALOMYELITIS
36	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
37	0	0	0	0	1	1	0	1	1	1	Para infectious	ACUTE DISSEMINAYED ENCEPHALOMYELITIS
38	0	0	0	0	0	0	0	0	0	1	Para infectious	DENGUE ENCEPHALITIS
39	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
40	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
41	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
42	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
43	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
44	0	0	0	0	0	0	0	1	0	0	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
45	0	0	0	0	0	0	0	1	1	0	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
46	0	0	0	0	0	0	0	0	1	0	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
47	0	0	0	0	0	0	0	1	1	1	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
48	0	0	0	0	0	0	0	1	1	1	Para infectious	ACUTE DISSEMINAYED ENCEPHALOMYELITIS
49	0	0	0	0	0	0	0	1	0	0	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
50	0	0	0	0	0	0	0	0	0	0	Para infectious	ACUTE NECROTIZING ENCEPHALITIS
51	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
52	0	0	0	0	0	0	0	1	1	0	Infectious	ENCEPHALITIS OF INFECTIVE ETIOLOGY
53	0	0	0	0	0	0	0	1	1	1	ACUTE LEUKOENCE	ACUTE LEUKOENCEPHALOPATHY WITH RESTRICTED DIFFUSION
54	0	0	0	0	0	0	0	0	0	1	ARACHNOID CYST	ARACHNOID CYST IN THE LEFT ANTERIOR TEMPORAL LOBE
55	0	0	0	0	0	0	0	0	0	0	PANSINUSITIS	PANSINUSITIS
56	0	0	0	0	0	0	0	1	1	1	POSTERIOR REVER	POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME
57	0	0	0	0	0	0	0	0	0	0	PANSINUSITIS	PANSINUSITIS
58	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
59	0	0	0	0	0	0	0	1	0	0	SEQULAE CHANGES	SEQULAE CHANGES TO NEONATAL HYPOXIMC ISCHEMIC INJURY
60	0	0	0	0	0	0	0	0	0	1	LEFT MESIAL TEM	LEFT MESIAL TEMPORAL SCLEROSIS
61	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
62	0	0	0	0	0	0	0	1	1	1	periventricular	periventricular and subcortical leukomalacia with cystic/gliotic changes
63	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
64	0	0	0	0	0	0	0	1	1	1	Para infectious	ACUTE LEUKOENCEPHALOPATHY? ROTAVIRUS INFECTION
65	0	0	0	0	0	0	0	0	0	0	Pansinusitis	PANSINUSITIS
66	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
67	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY
68	0	0	0	0	0	0	0	0	0	0	Normal	NORMAL STUDY

SL NO.	LABORATORY FINDINGS	T1	T2	FLAIR	DWI	SWI	ADC	MRS
1	CSF-SHOWED PLEOCYTES=255 CELLS/CU MM, ANTI MOG IgG=-VE, TLC-19,300, EEG-NORMAL	1	1	1	0	0	0	0
2	CSF-SHOWED PLEOCYTES=165 CELLS/CU MM, ANTI MOG IgG=-VE, TLC-20,340, GLUCOSE-99.0 mg/dl, PROTEINS-28.3 mg/dl, EEG-NORMAL	1	1	1	1	0	1	0
3	CSF-NORMAL STUDY, TLC-18,550, EEG-NORMAL	1	1	1	1	0	1	0
4	CSF-SHOWED PLEOCYTES=314 CELLS/CU MM, ANTI MOG IgG=-VE, TLC-29,450, EEG-DIFFUSE BIHEMISPHERIC DYSFUNCTION WITH SLOW WAVES	1	1	1	1	0	1	0
5	CSF-LACTATE=18.8, PROTEIN=399.8, GLUCOSE=49.0, TLC-23,200, LYMPHOCYTES-61%, NEUTROPHILS-39%, EEG- LOW VOLTAGE BI-PARIETAL SHARP WAVES SUGGESTIVE OF EPILEPTIFORM ACTIVITY	1	1	1	0	1	0	0
6	TLC-16,750, REST NOTHING SIGNIFICANT	0	0	0	0	0	0	0
7	CSF-NORMAL STUDY, PLATELET-15,000, TLC-30,000, EEG - diffuse bihemispheric dysfunction	1	1	1	1	1	1	0
8	CSF-NORMAL, EEG-BIHEMISPHERIC DYSFUNCTION	0	0	0	0	0	1	0
9	EEG-SHOWED ABNORMAL PERIODIC DISCHARGES, CSF-PLEOCYTOSIS =198 CELLS/CUMM, PROTEIN-114.2, GLUCOSE-36.2MG/DL	1	1	1	1	0	1	0
10	EEG- RIGHT HEMISPHERIC DYSFUNCTION, TLC-17,000, DENGUE-IgG & IgM +VE, NEUTROPHILIA, CSF-PROTEIN=311m/dl, glucose-32.omg/dl, lactate-15.2.	1	1	1	1	1	1	0
11	EEG-DIFFUSE BIHEMISPHERIC DYSFUNCTION WITH SLOW WAVES, DENGUE IgM & IgG-+VE, CSF-LYMPHOCYTES-71%, NEUTROPHILS-29%, CELLS-74 / CU MM	1	1	1	1	1	1	0
12	EEG-DIFFUSE BIHEMISPHERIC DYSFUNCTION WITH SLOW WAVES, ANTI-MOG ANTIBODIES=-VE	1	1	1	1	0	1	0
13	CSF-LACTATE=15.8, PROTEIN=105.8, GLUCOSE=59.0, TLC-13,200, EEG-NORMAL	1	1	1	0	0	0	0
14	CSF-SHOWED PLEOCYTES=287 CELLS/CU MM, ANTI MOG IgG=-VE, TLC-21,300, EEG,EEG- LOW VOLTAGE BI-PARIETAL SHARP WAVES SUGGESTIVE OF EPILEPTIFORM ACTIVITY	1	1	1	0	0	0	1
15	NOTHING SIGNIFICANT, CSF AND EEG NORMAL	0	0	0	1	0	1	0
16	CSF-LACTATE=31.8, PROTEIN=199.8, GLUCOSE=39.0, TLC-28.700, CELLS- 15/CU MM, LYMPHOCYTES-49%, NEUTROPHILS-51%, EEG-RECURRENT FRONTALLY DOMINANT EPILEPTIFORM DISCHARGES	1	1	1	1	1	1	0
17	EEG- LOW VOLTAGE BI-PARIETAL SHARP WAVES SUGGESTIVE OF EPILEPTIFORM ACTIVITY, CSF-PROTEIN=429 mg/dl, glucose-28.0mg/dl, lactate-19.0, RBC-61 CELLS	1	1	1	1	1	1	0
18	EEG- LOW VOLTAGE OCCIPITAL SHARP WAVES SUGGESTIVE OF EPILEPTIFORM ACTIVITY, CSF-PROTEIN=389 mg/dl, glucose-29.0mg/dl, lactate-18.0.	1	1	1	1	0	1	0
19	EEG-RECURRENT FRONTALLY DOMINANT EPILEPTIFORM DISCHARGES, CSF-PROTEIN-18.5, GLUCOSE-81.0, LACTATE-14.0	0	1	0	1	0	1	0
20	CSF-XANTHOCHROMIA+VE, RBC-126 CELLS, PROTEINS-330, GLUCOSE-31.2 MG/DL, EEG- SLOWED ABNORMAL PERIODIC DISCHARGES	1	1	1	1	1	1	0
21	CSF-NUCLEATED CELLS=300, PROTEINS=23.2, GLUSOSE=59.0 MD/DL, LYMPHOCYTES=98%, EEG-NORMAL	0	1	0	0	0	0	0
22	CSF-NORMAL STUDY, TLC-13,200 EEG-OCCASIONAL SHARP AND SLOW WAVE DISCHARGES OVER BILATERAL CENTROPARIETAL LEADS	0	1	1	0	0	0	0
23	TLC-22,550, EEG- BIHEMISPHERIC DYSFUNCTION, REST NOTHING SIGNIFICANT, CSF-NORMAL	1	1	1	0	0	0	0
24	EEG-DIFFUSE BIHEMISPHERIC DYSFUNCTION WITH SLOW WAVES, TLC-38,000, PLATELETS-85,000, CSF-LACTATE=31.8, PROTEIN=379.8, GLUCOSE=29.0	0	1	1	0	0	0	0
25	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
26	TLC-21,000, CSF-PLEOCYTOSIS-89 CELLS, LYMPHOCYTES-68%, NEUTROPHILS-32%, EEG-NORMAL	0	1	1	1	0	1	0
27	CSF-NORMAL, EEG-NORMAL	0	1	0	1	0	1	0
28	CSF-NORMAL, EEG-OCCASIONAL SHARP AND SLOW WAVE DISCHARGES OVER BILATERAL CENTROPARIETAL LEADS	1	1	1	0	0	0	0
29	anti MOG antibody= -ve, EEG-OCCASIONAL SHARP AND SLOW WAVE DISCHARGES OVER BILATERAL CENTROPARIETAL LEADS, CSF-NORMAL	0	1	1	0	0	0	0
30	CSF-XANTHOCHROMIA+VE, RBC-112 CELLS, PROTEINS-56, GLUCOSE-91.2 MG/DL, DENGUE IgM & IgG +VE, PLATELETS-31,000, EEG-BIPARIETAL PERIODIC SHARP WAVES SUGGESTIVE OF EPILEPTIFORM ACTIVITY	0	1	1	1	1	1	0
31	CSF- PLEOCYTOSIS-98 CELLS, LYMPHOCYTES-26%, NEUTROPHILS-74%, PROTEINS-214.2, GUCOSE-28.6 MG /DL, CSF PCR- NOT DONE, EEG-EEG-OCCASIONAL SHARP AND SLOW WAVE DISCHARGES OVER BILATERAL CENTROPARIETAL LEADS	0	1	1	0	0	0	0
32	CSF- PLEOCYTOSIS-106 CELLS, LYMPHOCYTES-76%, NEUTROPHILS-24%, PROTEINS-44.2, GUCOSE-98.6 MG /DL, CSF PCR- NOT DONE, EEG-PERIODIC SHARP WAVES IN BILATERAL PARIETO-TEMPORAL REGIONS SUGGESTIVE OF EPLILEPTIFORM ACTIVITY	0	1	1	0	0	1	0
33	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
34	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
35	EEG-NORMAL, PERIPHERAL SMEAR- HEMOLYIC ANAEMIA WITH NEUTROPHILIA, TLC-7120, CSF-NORMAL	0	1	1	0	0	0	0

36	EEG- BIHEMISPHERIC DYSFUNCTION	0	0	0	0	0	0	0
37	MOG ANTIBODY POSITIVE, CSF- GLUCOSE-102.6, PROTEIN-25.3, NO CELLS, EEG-PERIODIC BIHEMISPHERIC SHARP WAVES SUGGESTIVE OF EPILEPTIFORM ACTIVITY	0	1	1	0	0	0	0
38	CSF- PROTEINS-13.4, GLUCOSE-104.4 MG/DL, DENGUE IgM & IgG +VE, PLATELETS-25,100, EEG- DIFFUSE BIFRONTOPARIETAL SLOW WAVES	0	1	1	1	0	1	0
39	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
40	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
41	CSF-LACTATE=15.8, PROTEIN=105.8, GLUCOSE=59.0, TLC-13,200, LYMPHOCYTES-67%, EUTROPHILS-33%, EEG-NORMAL	0	0	0	0	0	0	0
42	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
43	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
44	TLC-27,500, CSF-NORMAL STUDY, EEG-NORMAL	0	1	0	0	0	0	0
45	EEG - RIGHT HEMISPHERIC DYSFUNCTION, CSF-NORMAL	0	1	1	0	0	0	0
46	TLC-22,540, CSF-LYMPHCYTES-5%, NEUTROPHILS-95%, PROTEINS-220.9 mg/dl, GLUCOSE-42.0 mg/dl, EEG-NORMAL	0	1	1	0	0	0	0
47	TLC-22,800, CSF-LYMPHCYTES-5%, NEUTROPHILS-95%, PROTEINS-280.9 mg/dl, GLUCOSE-32.0 mg/dl, EEG-DIFFUSE BIHEMISPHERIC DYSFUNCTION	0	1	1	0	0	0	0
48	anti MOG antibody= -ve, anti-aquaporin-4 IgG=-VE, TLC-18,700, CSF-LYMPHCYTES-95%, NEUTROPHILS-5%, PROTEINS-38.9 mg/dl, GLUCOSE-72.0 mg/dl, EEG- NORMAL	1	1	1	0	0	0	0
49	CSF-NUCLEATED CELLS=300, PROTEINS=23.2, GLUSOSE=59.0 MD/DL, LYMPHOCYTES=98%, EEG-NORMAL	0	1	1	0	0	0	0
50	EEG- LOW VOLTAGE BI-PARIETAL SHARP WAVES SUGGESTIVE OF EPILEPTIFORM ACTIVITY, CSF-PROTEIN=399 mg/dl, glucose-17.0mg/dl, lactate-39.0, RBC-48 CELLS/CU MM	0	1	1	0	1	0	0
51	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
52	CSF-NORMAL, EEG-NORMAL	0	1	1	0	0	0	0
53	CSF-NORMAL LIMITS, CSF INTERLEUKIN/ANTI-MOG/AQUA-PORIN ANTIBODIES-NOT AVAILABLE, EEG-DIFFUSE BIHEMISPHERIC DYSFUNCTION	0	0	0	1	0	1	1
54	NOTHING SIGNIFICANT	1	1	1	1	0	1	0
55	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
56	NOTHING SIGNIFICANT	0	1	1	0	0	0	0
57	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
58	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
59	TLC-15,800, CSF-LACTATE-92 MG/DL, PROTEINS-116.4, GLUCOSE-22.6 MG/DL, NO CELLS, EEG-ABNORMAL	0	1	1	0	0	0	0
60	EEG - SHOWS SHARP AND SLOW WAVES IN THE LEFT TEMPORO-OCCIPITAL LOBES, CSF-NORMAL	0	1	0	0	0	0	0
61	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
62	CSF-LACTATE=62.8, PROTEIN=124.8, GLUCOSE=39.0, TLC-16,200, LYMPHOCYTES-67%, EUTROPHILS-33%, EEG-ABNORMAL	0	1	1	0	0	0	0
63	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
64	CSF-NUCLEATED CELLS=300, PROTEINS=23.2, GLUSOSE=59.0 MD/DL, LYMPHOCYTES=98%, EEG-DISSFUSE BIHEMISPHERIC DYSFUNCTION	0	1	1	1	0	1	0
65	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
66	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
67	NOTHING SIGNIFICANT	0	0	0	0	0	0	0
68	NOTHING SIGNIFICANT	0	0	0	0	0	0	0

Introduction



Objectives

Review of Literature

Methodology

Results

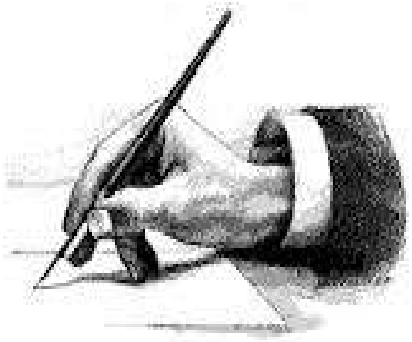
Discussion

Conclusion

Limitations

Summary

Bibliography



Annexure-I

Annexure-II

Annexure-III

Annexure-IV

Annexure-V

Annexure-VI