

## Research Article

# Early vs. Delayed Neuroimaging in Children with Non-Traumatic Acute

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**Abstract:** Introduction Encephalopathy is a term that means brain disease, damage, or malfunction. Encephalopathy can present a very broad spectrum of symptoms that range from mild, such as some memory loss or subtle personality changes, to severe, such as dementia, seizures, coma or death. In general, encephalopathy is manifested by an altered mental state that is sometimes accompanied by physical manifestations (for example, poor coordination of limb movements). The diagnosis of encephalopathy is usually made with clinical tests done during the physical examination (mental status tests, memory tests, and coordination tests) that document an altered mental state. In most cases, findings on clinical tests either diagnose or presumptively diagnose encephalopathy. Usually, the diagnosis is achieved when the altered mental state accompanies another primary diagnosis such as chronic liver disease, kidney failure, anoxia, or many other diagnoses. **Materials & Methods** This is a Prospective observational study conducted in the Inpatient Department of Paediatric, Tertiary Care Teaching Hospital. MRI/CT brain will be performed according to the clinical requirement and patient condition at initial admission. If there is clear diagnostic information on initial imaging no further neuroimaging will be performed on these children unless a prognostic imaging is deemed necessary by treating neurologist. Delayed imaging will be done when the initial neuroimaging is normal/nondiagnostic and child continues to have neurological symptoms and signs without obvious diagnoses from clinical, blood, CSF investigations. Also, when there are new onset neurological symptoms/ progressive worsening of neurological status after initial neuroimaging. **Result** In 21.95% of cases, second scan was done on 4th day of illness followed by 12.19% of cases on 3rd day. Second scan was done from 4th-10th day of illness in 56.09% followed by 1st-3rd day and 11th -20th day in 19.51% and 17.07% respectively. Second scan was diagnostic in 80.48% of cases and nonspecific findings in 4.87% of cases and was normal in only 4.87% of cases. Reason for second neuroimaging was Clinical Worsening in 41.46% and No Clinical Improvement in 31.7% of cases. Second neuroimaging was Diagnostic in 9.75% of cases. Delayed neuroimaging and Both Neuroimaging were equally helpful in majority of cases (78.04%) and no neuroimaging was helpful in 17.07% of cases. First neuroimaging was diagnostic in 46.34% of cases and not diagnostic in 56.68% of cases. Second neuroimaging was diagnostic in 60.97% of cases and nondiagnostic in 34.14% of cases. **Conclusions** The present study demonstrates that there is a subjective component to scan interpretation, which can have important implications for the clinical management of acute encephalopathy cases. The agreement between raters was good for CT but only moderate for MRI. Agreement varied with diagnosis; for blinded reading radiologists were good at diagnosing acute encephalopathy; however, agreement was worse for ADEM and other alternative aetiologies. The study showed that imaging data are affected by imaging timing and technique, and there was poor agreement on some regional abnormalities.

**Keywords:** Non-Traumatic Acute Encephalopathy, Early Neuroimaging, Delayed Neuroimaging.

## INTRODUCTION

Encephalopathy is a term that means brain disease, damage, or malfunction. Encephalopathy can present a very broad spectrum of symptoms that range from mild, such as some memory loss or subtle personality changes, to severe, such as dementia, seizures, coma or death. [1] In general, encephalopathy is manifested by an altered mental state that is sometimes accompanied by physical manifestations (for example, poor coordination of limb movements). [2]

Despite the numerous and varied causes of encephalopathy, at least one symptom present in all cases is an altered mental state. The altered mental state may be subtle and develop slowly over years (for example, the decreased ability to draw simple designs, termed apraxia) termed as chronic encephalopathy or be profoundly obvious and develop rapidly (for example,

brain anoxia leading to coma or death in a few minutes) termed as acute encephalopathy. [4]

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The diagnosis of encephalopathy is usually made with clinical tests done during the physical examination (mental status tests, memory tests, and coordination tests) that document an altered mental state. In most cases, findings on clinical tests either diagnose or presumptively diagnose encephalopathy. Usually, the diagnosis is achieved when the altered mental state accompanies another primary diagnosis such as chronic liver disease, kidney failure, anoxia, or many other diagnoses. [6]

Consequently, paediatric neurologists may utilize several different tests at the same time to diagnose both the primary condition (the cause of encephalopathy) and

the encephalopathy itself. This approach to diagnosis is done by most physicians, because encephalopathy is a complication that occurs because of a primary underlying health problem. The most frequently utilized tests are listed below with some of the major primary causes the tests may help diagnose: [7]

Choice of investigation, including neuroimaging modality, can be a daunting prospect for the clinician faced with the encephalopathic child and it is important to select appropriately for a high diagnostic yield. [8]

Etiology of nontraumatic acute encephalopathy, age at the insult and clinical status at the time of presentation are likely predictors of outcome.

A better understanding of causes and outcome is essential to help to improve the approach and to plan rational management of nontraumatic acute encephalopathy.

## METHODOLOGY & MATERIALS

- Inpatient Department of Paediatric, Tertiary Care Teaching Hospital.
- Study Population
- Children between 1-month and 18 years of age.

### Inclusion Criteria

Patients meeting the following criteria will be included into the study:

1. Children between 1-month and 18 years of age.
2. Children with status epilepticus and acute encephalopathy.
3. Children with acute encephalopathy with GCS  $\leq$  13

### Exclusion Criteria

Patients meeting ANY of the following exclusion criteria will be excluded from the study:

1. Children below 1 month and above 18 years of age.
2. Children with history of head trauma.
3. Children with previous non-progressive structural anomalies
4. Toxin ingestion

### Study Design

#### Prospective observational study.

MRI/CT brain will be performed according to the clinical requirement and patient condition at initial admission. If there is clear diagnostic information on initial imaging no further neuroimaging will be performed on these children unless a prognostic imaging is deemed necessary by treating neurologist.

Delayed imaging will be done when the initial neuroimaging is normal/nondiagnostic and child continues to have neurological symptoms and signs

without obvious diagnoses from clinical, blood, CSF investigations. Also, when there are new onset neurological symptoms/ progressive worsening of neurological status after initial neuroimaging.

Early scan is defined as  $\leq$  3 days from the point of neurological symptom onset.

Delayed scan is defined as  $\geq$  3 days from the point of neurological symptom onset.

Who will get the delayed imaging? - Children who continue to be encephalopathic or continue to have seizures without diagnostic information on initial scan or other diagnostic modalities (like haematological investigations, CSF analysis). Repeat imaging will be performed according to the clinical judgement based on the paediatric neurologist's discretion.

### Method and Data Collection

1. Paediatrician/neurologist(s) will assess all the children presenting with acute encephalopathy and screen them after obtaining a written informed consent from the respective parent and assent from the eligible patients (aged  $>$ 7 years). The demographic, pre hospital data, clinical history and examination details of enrolled children will be entered in a pre-designed structured proforma.
2. This assessment will be made by the paediatrician/neurologist on inpatient basis.
3. The radiological images and findings will be reviewed by a radiologist on prospective basis

### Statistical Methods

The data for the present study will be collected retrospectively from the hospital records and on pre designed format for prospective cases. The data will be entered into MS-Excel for further analysis. The results will be expressed as median and Inter quartile Range (IQR) for continuous variables.

The categorical variables will be expressed as percentage (%), frequency distribution. Appropriate non-parametric tests like chi square and Fishers exact tests will be applied. The analysis will be carried out by using Statistical Package for Social Sciences (SPSS20th version). A p value of  $<$ 0.05 with two sided will be considered as statistically significant.

### Ethical Consideration

The study will be initiated after obtaining approval from Ethics Committee.

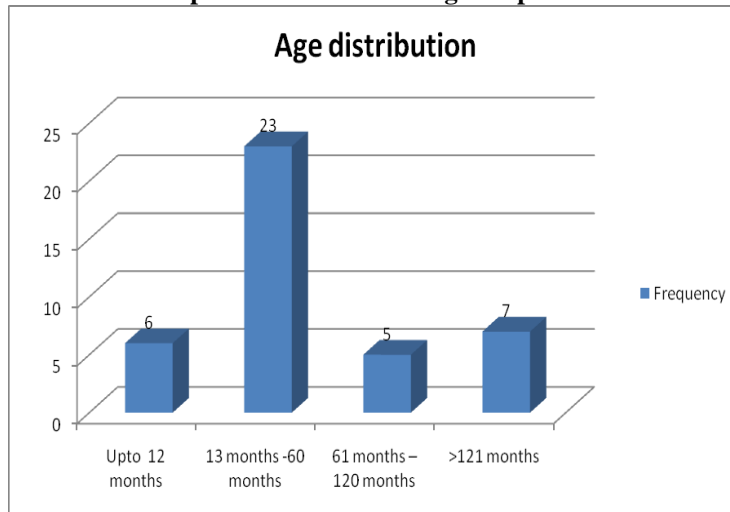
This is an observational study based on data collection and clinical examination. Prospective patients will be screened only after obtaining a written informed consent

from their respective parents and assent from the eligible patients (aged >7 years).

## RESULT

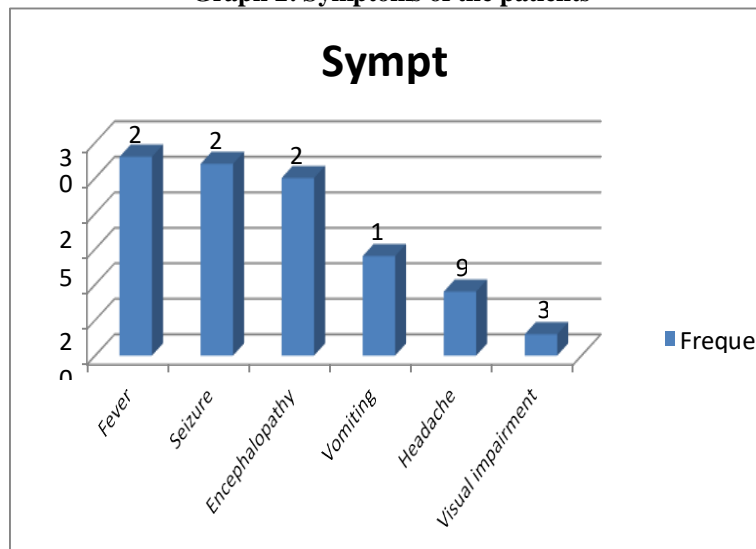
Maximum number of patients were in the age group of 13 to 60 months (56%) followed by 17% in >121 months age group and least number of patients were in 61 to 120 months age group (12.2%).

**Graph 1: Distribution of age the patients**



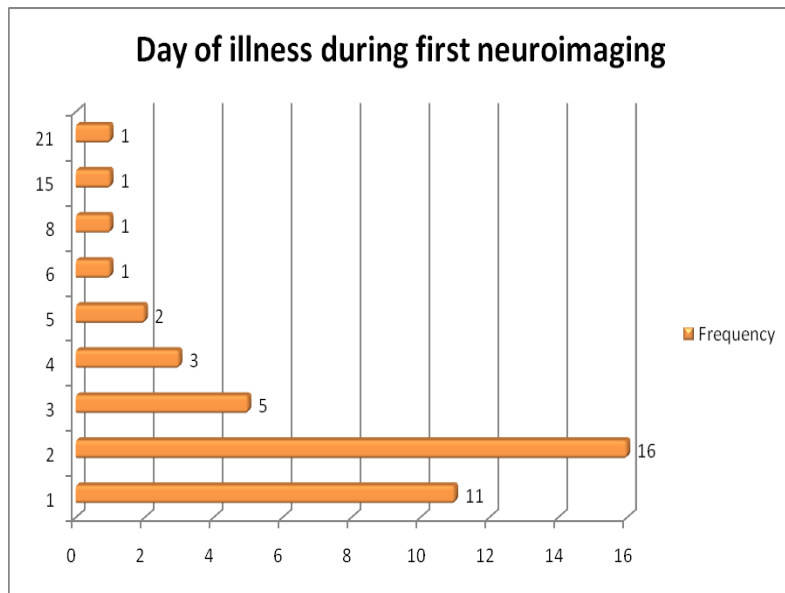
Highest percentage of symptom was fever (68.29%) followed by seizure (65.85%) and encephalopathy (60.9%). Vomiting was in 34.14% of patients. Lowest percentage of symptom was Visual impairment. (21.95%).

**Graph 2: Symptoms of the patients**



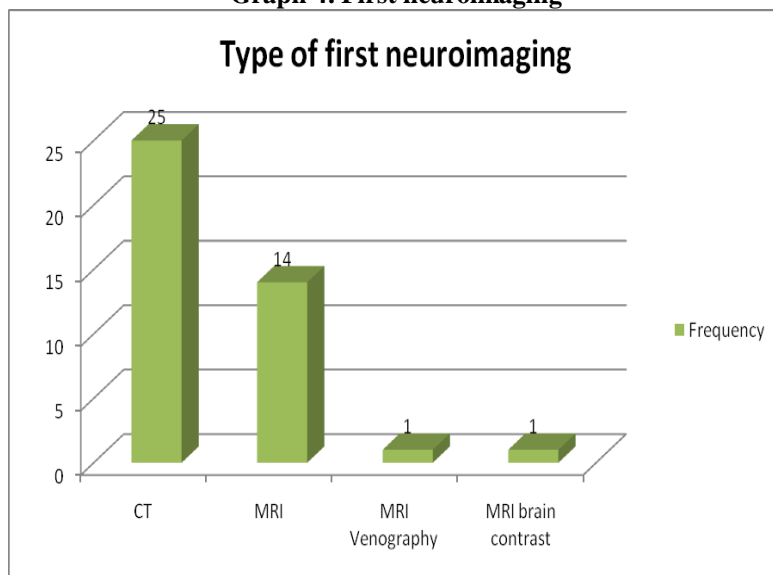
In 39.02 % of cases, first neuroimaging was done on Day-2 of illness and in 26.82% of cases, it was done on Day-1 of illness followed by 12.19% of patients on 3rd day of illness.

**Graph 3: Day of illness during first neuroimaging**



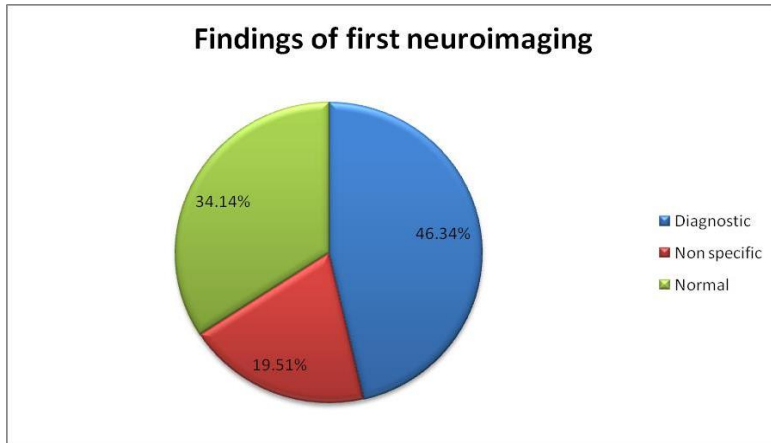
In 60.97% of cases, type of first neuroimaging in our study was CT head plain whereas in 34.14% of cases MRI head plain was done. MRI brain Venography and MRI brain with contrast was done in only 2.43% of cases.

**Graph 4: First neuroimaging**



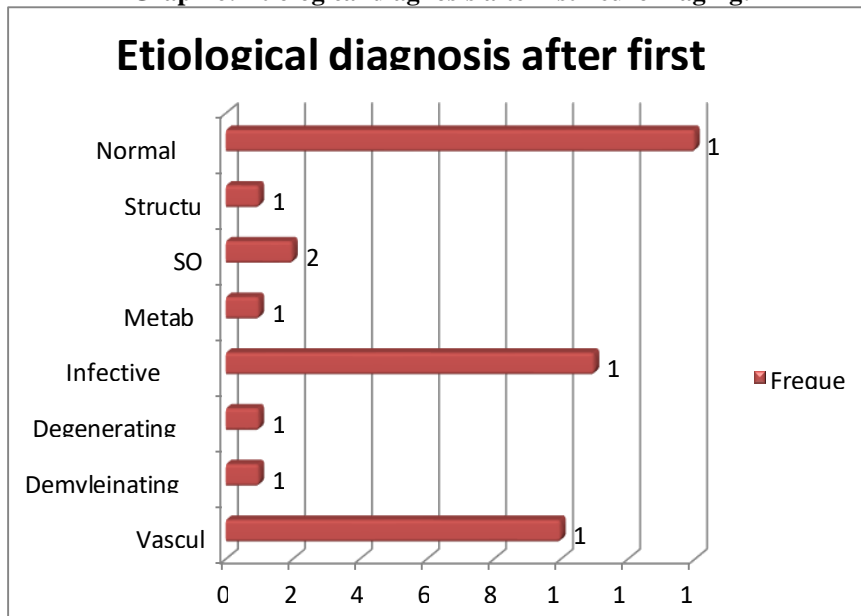
In 46.34% of cases, first neuroimaging was diagnostic and in 34.14% of cases, it was normal and nonspecific findings were in 19.51% of cases.

**Graph 5: Findings of first neuroimaging:**



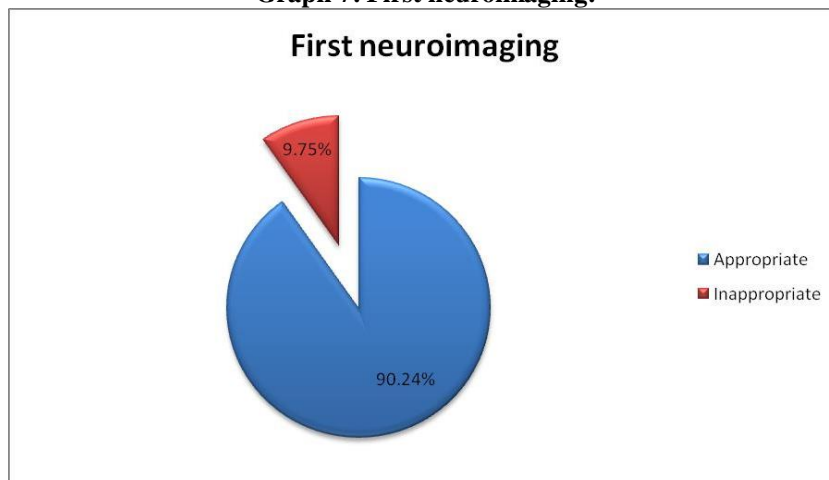
In 34.14% of cases, first neuroimaging was normal whereas there was infective etiology in 26.82% of cases and vascular etiology in 24.3% of cases.

**Graph 6: Etiological diagnosis after 1st neuroimaging:**



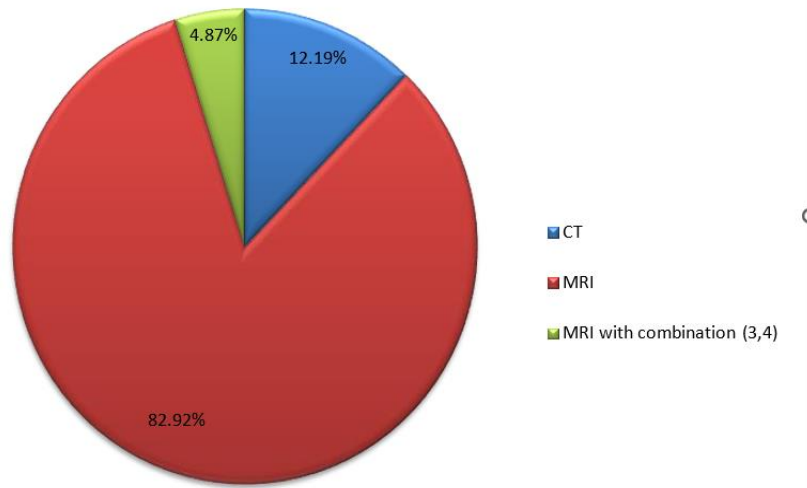
In majority of cases (90.24%), first neuroimaging was Appropriate and was Inappropriate in only 9.75% of cases.

**Graph 7: First neuroimaging:**



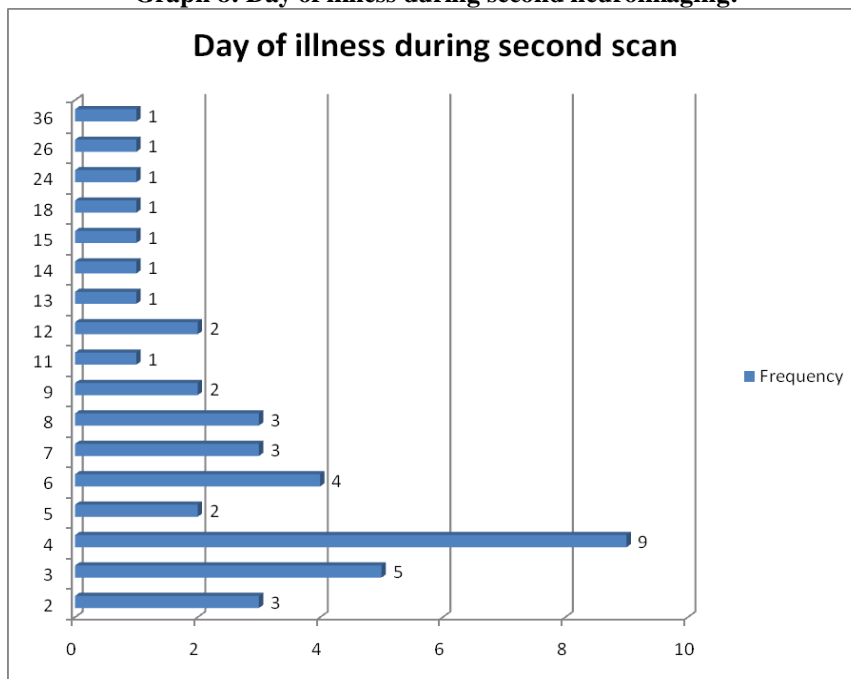
In majority of cases (82.92%), first neuroimaging was plain MRI head and CT scan was done in only 12.19%.

**Graph 8: Nature of scan:  
Type of second scan**



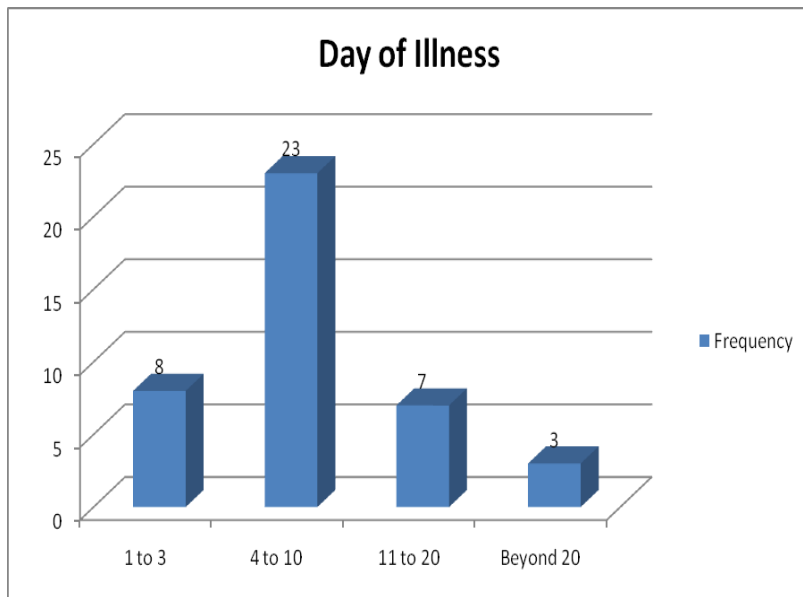
In 21.95% of cases, second scan was done on 4th day of illness followed by 12.19% of cases on 3rd day.

**Graph 8: Day of illness during second neuroimaging:**



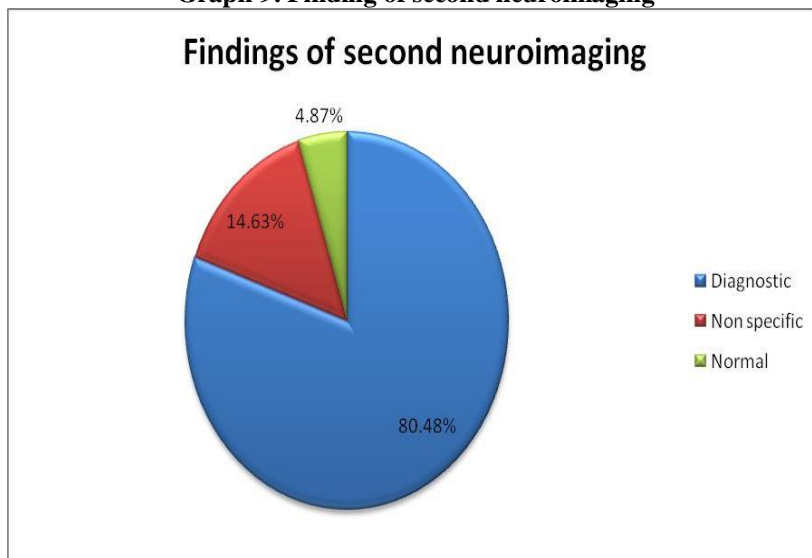
Second scan was done from 4th-10th day of illness in 56.09% followed by 1st-3rd day and 11th -20th day in 19.51% and 17.07% respectively.

**Graph 9: Day of illness**



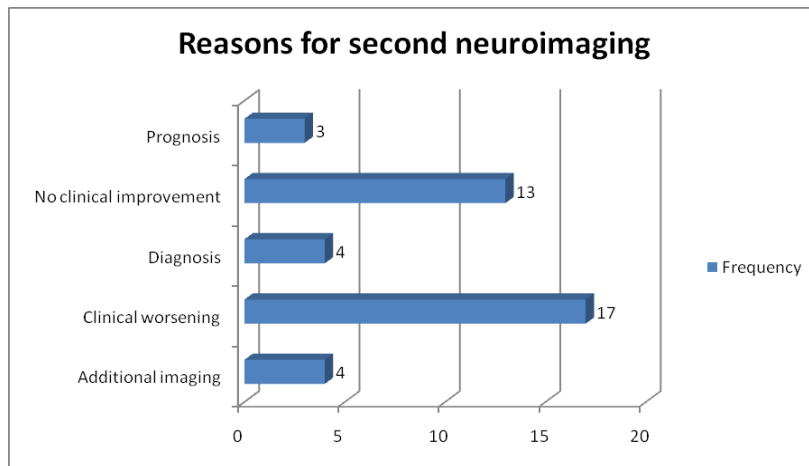
Second scan was diagnostic in 80.48% of cases and nonspecific findings in 4.87% of cases and was normal in only 4.87% of cases.

**Graph 9: Finding of second neuroimaging**



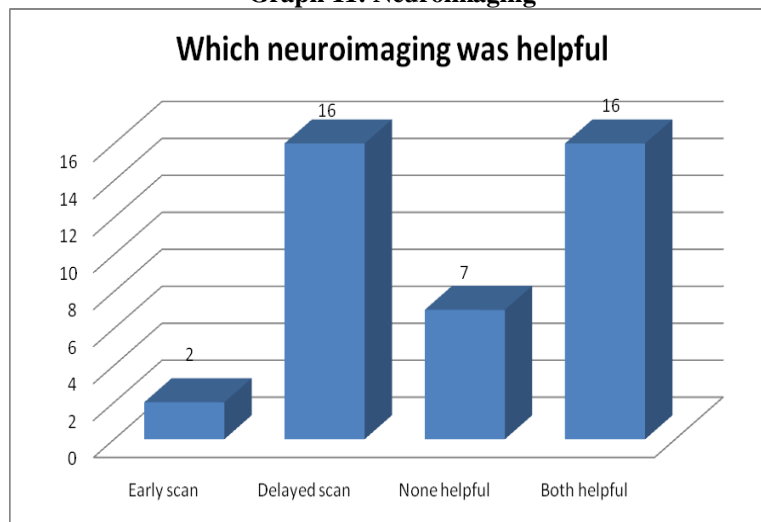
Reason for second neuroimaging was Clinical Worsening in 41.46% and No Clinical Improvement in 31.7% of cases. Second neuroimaging was Diagnostic in 9.75% of cases.

**Graph 10: Reasons for second neuroimaging**



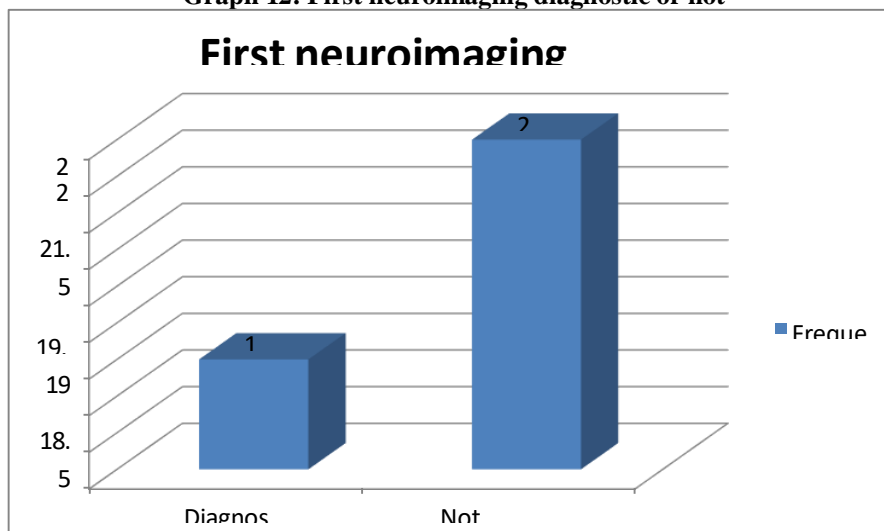
Delayed neuroimaging and Both Neuroimaging were equally helpful in majority of cases (78.04%) and no neuroimaging was helpful in 17.07% of cases.

**Graph 11: Neuroimaging**



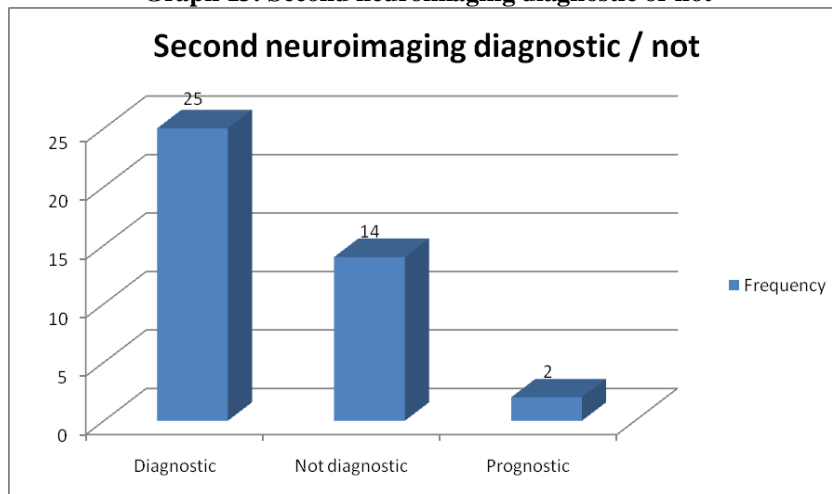
First neuroimaging was diagnostic in 46.34% of cases and not diagnostic in 53.66% of cases.

**Graph 12: First neuroimaging diagnostic or not**



Second neuroimaging was diagnostic in 60.97% of cases and nondiagnostic in 39.03% of cases.

**Graph 13: Second neuroimaging diagnostic or not**



## DISCUSSION

In our study after fever (68.29%), which are diagnostic criteria for acute Encephalopathy is Seizure (65.85%) were the major complaints, while vomiting were the most common symptoms on clinical examination present 34.14% of cases. According to Nishiyama M et al

Cases with viral etiologies had seizure, refusal of feeds, involuntary movements, GCS < 8, dystonia, and focal deficit as predominant clinical features. Similar clinical features were also observed in viral encephalitis cases by Karmakar et al.[9] Vomiting and meningeal signs were more prominent in pyogenic cases whereas CNS TB presented with headache, raised ICP, cranial nerve palsy, and dystonia. Meningeal signs were conspicuously absent in cerebral malaria. [10]

Data on the yield of neuroimaging in children with Encephalopathy is limited. In one review of neuroimaging data for children with Encephalopathy, structural lesions that would likely be detected by neuroimaging were present 25 (60.97%) with CT head plain and with 14 (34.14%) MRI head plain corresponding to lesions we would classify as urgent or emergent intracranial pathology. However, all of these children underwent neuroimaging. According to one study, actual neuroimaging data was only available for 198 children (174 CT and 24 MRI) on another hand from six studies with a mean of 49% abnormal (range 29–70%). 31 However, these data were not limited to children with Encephalopathy.

In a second study examining 144 children with Encephalopathy as a presentation of new-onset seizure, the combination of CT and MRI identified an underlying reason for SE in 30% of which 10% were described as “acute” abnormalities.<sup>11</sup> A recent analysis found that 11% of children with new unprovoked seizure had neuroimaging abnormalities but only 0.8% representing emergent findings. This study however only included 11% of patients with seizure > 15 minutes, and seizure

duration > 15 minutes was associated with an increased incidence of abnormal neuroimaging findings.<sup>12</sup>

In our study, infective Etiological diagnosis after 1st neuroimaging. Vascular Etiological was 24.3% and Demyelinating disease, Degenerative disease, Metabolic and Structural were 2.43%. This could be explained by the great increase in the incidence of Acute Encephalopathy in the recent years in India, and the study population is belonging to a state with high burden for both the infections. [13] Recent studies also indicate an increasing prevalence of Acute Encephalopathy across the globe. [14]

According to Kneen R et al [15] only in about 60% of cases etiology could be ascertained in his study. The probable reasons for such a big proportion of cases remaining etiologically inconclusive could be many, and includes: (i) specific serological and molecular-based investigations for many viral agents known to cause AFE in children (e.g., human herpesvirus 6, West Nile virus, etc.) were not done;

(ii) many cases of bacterial meningitis may have received over the counter antibiotics making the CSF bacteriologically sterile and difficult to interpret, and latex agglutination test for pneumococcus, Haemophilus influenzae or Neisseria meningitidis was not done in such cases; (iii) nonavailability of investigations for autoimmune encephalitis (e.g. CSF anti-N-methyl-D-aspartate receptor antibody, Anti-voltage gated potassium channel antibody, etc.). [16]

However, again, in the earlier study by Kumar et al., even with extensive investigations for Acute Encephalopathy 40% cases remained etiologically unexplained. [17] The above-mentioned investigations are also not routinely available in most of the secondary and tertiary level health-care facilities of India and other developing countries, where such patients are being managed. The almost similar pattern of distribution of etiological diagnosis was in a recent study from central

India. [3] Although the spectrum remains the same, the most common cause seems to vary according to the geographical region depending on the endemicity of different infective agents, with viral causes being predominant in Asia. [18]

## CONCLUSION

This study has highlighted some of the disease processes that produce diagnostic difficulty in the emergency neuroradiology setting. Because radiologists are often the first individuals to consider these entities, they must be familiar with the clinical features that suggest the diagnosis. Furthermore, acquaintance with the various imaging findings of these diseases will allow earliest diagnosis and will help limit the severe complications that follow these neurologic emergency conditions if left untreated.

In conclusion, the present study demonstrates that there is a subjective component to scan interpretation, which can have important implications for the clinical management of acute encephalopathy cases. The agreement between raters was good for CT but only moderate for MRI. Agreement varied with diagnosis; for blinded reading radiologists were good at diagnosing acute encephalopathy; however, agreement was worse for ADEM and other alternative aetiologies. The study showed that imaging data are affected by imaging timing and technique, and there was poor agreement on some regional abnormalities. The findings of the present study support the current UK guidance dismissing the diagnosis of acute encephalopathy when the MRI is normal 72 hours after neurological symptom onset with appropriate negative CSF tests. Further research is needed to better define common radiological abnormalities in order to define diagnostic criteria for acute encephalopathy diagnoses.

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