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A Prospective Observational Study Utility Of Mri In Identifying Possible Etiology Of Epilepsy In Paediatric Population

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Abstract

Background : Neuroimaging is important for determining etiology and guiding care in early childhood epilepsy. However, access to appropriate imaging in sub-Saharan Africa is modest, and as a consequence, etiological descriptions of childhood epilepsy in the region have been limited. We sought to describe MRI findings in children with epilepsy presenting to a tertiary hospital.

Aim of the study : To assess prevalence of structural abnormalities identified with MRI in epileptic patients.To obtain correlation between structural abnormalities and clinical presentation of epilepsy.

Methods : **:** The study was conducted in the year 2021,in Department of Radiodiagnosis, in collaboration with department of Peadtrics, Apollo Hospitals, Hyderabad, Telangana, India. A study population of 216 children were selected according to the following inclusion and exclusion criteria. History regarding seizure episodes was obtained which included seizure semiology, pharmacotherapy and any other associated symptoms. Family history of seizure was also elicited.After this, elaborate neurological examination was done and any obvious neurological deficits were recorded.Review and documentation of investigations.

Results : The mean age of the study population was 5.5 ± 2.6 years. The study population age group ranged from 3 months to 12 years. In our study population 92 patients had structural lesions in MRI which accounts for 42.6% of the total study population. Among those patients 41 patients (44 %) had focal lesions and 51 (56 %) patients had multifocal or generalised lesions. Among the study population 70 patients (32.4 %) had focal seizure episodes on onset of clinical seizures, 130 patients (60.2 %) had generalised seizure episodes on onset and in 16 patients (7.4 %) the onset was not well defined.When analysing the clinical course of patients with focal seizures (n = 70), 39 patients continued to have focal seizures alone and in 31 patients had secondary generalised seizures. So the ultimate clinical seizure episode was focal in 39 patients and generalised (primary generalised + secondary generalised) in 177 patients. The association between locations of MRI findings were analysed against the clinical onset of seizures. Patients with multifocal lesions and generalised lesions were clumped together. There was significant association between (p-0.000) MRI lesions and the seizure onset. Patients with focal lesions have significantly higher incidence of focal onset of seizures and patients with multifocal / generalised lesions have higher incidence of generalised onset of seizures. Among the patients with MRI findings, 44 patients had EEG data. Association between MRI findings and EEG findings were analysed. There was significant association between focal changes in MRI and focal EEG abnormalities (p-0.000). Similarly multifocal / generalised MRI findings were associated with multifocal / generalised EEG abnormalities.Spearman correlation also confirmed the positive correlation between MRI and EEG findings (p-0.000).

Conculsion : The MRI was able to identify brain lesions in 38% of pediatric patients who presented with seizures. The study revealed inflammatory granuloma as the commonest cause of seizures in children, followed by Hypoxic-Ischemic Injury. Early recognition of potentially treatable diseases helps in timely treatment and arrest of disease progression. It is recommended to use MRI as a primary investigation during the evaluation and management of pediatric seizures.

Keywords: Hypoxic ischemic injury, Inflammatory granuloma, Neurocysticercosis, Seizures

Introduction

Epilepsy is a disorder characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition. It is one of the common and frequently encountered neurological conditions that imposes significant burden on individuals, families, and also on healthcare systems.[1] Patients with conditions like, developmental malformations of brain tissue (cortex), loss of blood supply and infarctions occurring during birth (perinatal infarctions), Tumours, scarring of brain tissue (Mesial temporal sclerosis), infections, inflammatory and immunologic conditions (Eg: Rassmusen encephalitis) and congenital disorders involving the brain (Eg: Neurocutaneous syndromes) are shown to have definitive structural abnormalities in the brain leading to development of seizures. Identification of these lesions with radiological modalities will help in early determination of treatment options in these patients.[2]Among the various modalities available to image the brain, Magnetic resonance imaging (MRI) is currently the mainstay of diagnosing abnormalities of brain in epilepsy patients.[3] It is non invasive, painless and has no ionization hazards. It is also highly sensitive in diagnosing the scarring of brain (Sclerosis), loss of brain tissue (Hippocampal volume loss) and in parasitic infestations. However MRI is expensive when compared to other imaging modalities and electrophysiological techniques. Studies have shown that the prevalence of structural lesions in brain that predisposes to epilepsy differs from developed and developing countries and also between geographical regions in same country.[4] Diagnosis of epilepsy is based on clinical assessment, Electro encephalography (EEG) findings and neuroimaging. The history provided by the witness and the experience and skill of neurologist are important for clinical judgement.[5] Although EEG provides valuable clue there are only few centres available in developing countries that provide comprehensive EEGlaboratories providing correct diagnosis. Neuroimaging including CT scan and MRI can provide valuable clue in diagnosis.[6] Although MRI is sensitive for structural lesions the utility of MRI in identifying aetiology of epilepsy is not well defined as the structural lesions vary from region to region.[7]

Methods : The study was conducted in the year 2021,in Department of Radiodiagnosis, in collaboration with department of Peadtrics, Apollo Hospitals, Hyderabad, Telangana, India. A study population of 216 children were selected according to the following inclusion and exclusion criteria. History regarding seizure episodes was obtained which included seizure semiology, pharmacotherapy and any other associated symptoms. Family history of seizure was also elicited.After this, elaborate neurological examination was done and any obvious neurological deficits were recorded.Review and documentation of investigations.Inclusion criteria: Age 1 month to 12 years of both genders.Underwent MRI as part of evaluation for seizure disorder. Exclusion criteria: Patient‟s relatives not giving consent. Pseudoseizures. Seizures with head injury. Acute CNS infection.Neonatal seizures.

Mri - Epilepsy Protocol

1. T1-weighted MPRAGE or SPGR images from nasion to inion
2. 1.5mm slice thickness with no intervening gap
3. 3D imaging for post-processing into multiple planes
4. Coronal and axial FLAIR sequences with a 2- to 3-mm slice thickness and a 0- to 1-mm interslice gap.

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5. T2-weighted, axial and coronal sequence with 3mm slice thickness

Statistical Analysis: Microsoft excel 2016 was used to tabulate and compute variables.SPSS version 16 (SPSS Inc, Chicago, 2007) was used for statistical analysis. Chi square test will be used to assess the association. Fisher‟s exact test will be used when any observation is less than 5. A p value of <0.05 will be considered as significant relationship between two variables. Spearman correlation was used to assess for correlation between two variables. Values between 0 to +1 and p<0.05 will be considered as positive correlation.

Results

TABLE AGE DISTRIBUTION

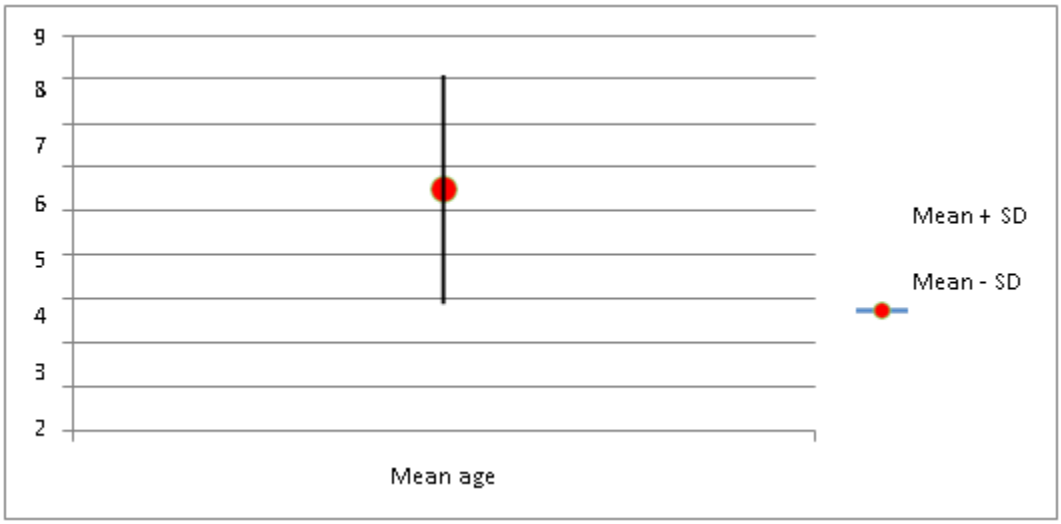

Table :1 The mean age of the study population was 5.5 ± 2.6 years. The study population age group ranged from 3 months to 12 years

Table :2 MRI FINDINGS

MRI findings in focal lesions	Number	Percentage (n-92)
Focal lesions		
Focal cerebral atrophy	4	4.3 %
Focal gliosis	15	16.3 %
Mesial temporal sclerosis	4	4.3 %
Focal cortical dysplasia	3	3.2 %
Tuberculoma	12	13 %
Neurocysticercosis	3	3.2 %
Generalised / Multifocal lesions		
Corpus callosum agenesis	2	2.1 %
B/L Cerebellar atrophy	1	1.1%
Diffuse cerebral atrophy	17	18.4 %
Hydrocephalus	3	3.2 %

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Diffuse gliosis	8	8.6 %
Periventricular leukomalacia	8	8.6 %
Basal ganglia hyperintensity	8	8.6 %
Cortical tuber / Angiomatosis	4	4.3 %

Table :2 In our study population 92 patients had structural lesions in MRI which accounts for 42.6% of the total study population. Among those patients 41 patients (44 %) had focal lesions and 51 (56 %) patients had multifocal or generalised lesions

TABLE :3 CLASSIFICATION OF SEIZURE:

	FOCAL	GENERALISED	UN KNOWN	TOTAL
ONSET	70 (32.4%)	130 (60.2%)	16 (7.4%)	216
Clinical course	39 (18.1%)	177 (81.9%)	--	216

Table :3 Among the study population 70 patients (32.4 %) had focal seizure episodes on onset of clinical seizures, 130 patients (60.2 %) had generalised seizure episodes on onset and in 16 patients (7.4 %) the onset was not well defined.When analysing the clinical course of patients with focal seizures (n = 70), 39 patients continued to have focal seizures alone and in 31 patients had secondary generalised seizures. So the ultimate clinical seizure episode was focal in 39 patients and generalised (primary generalised + secondary generalised) in 177 patients.

Table :4 PHARMACOTHERAPY:

No of drugs used	1	2	3	4	TOTAL
Number of patients	62	106	35	13	216
percentage	28.7 %	49.1 %	16.2 %	6 %	100 %

Table :4 The number of drugs used in each patient was computed. Single drug was used in 62 patients and multiple drugs were used in rest of the patients.

TABLE :5 MRI FINDINGS AND SEIZURE ONSET:

	Focal onset	Generalised onset	Unknown	Total
Focal lesion in MRI	27 (65.8 %)	11 (26.8 %)	3 (7.3 %)	41
Multifocal / Generalised lesions in MRI	7 (13.7%)	42 (82.3 %)	2 (3.9 %)	51

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Fishers exact test; p - 0.000

The association between locations of MRI findings were analysed against the clinical onset of seizures. Patients with multifocal lesions and generalised lesions were clumped together. There was significant association between (p-0.000) MRI lesions and the seizure onset. Patients with focal lesions have significantly higher incidence of focal onset of seizures and patients with multifocal / generalised lesions have higher incidence of generalised onset of seizures.

TABLE :6 MRI FINDINGS AND CLINICAL COURSE OF EACH SEIZURE EPISODE:

	Focal	Secondary generalised & Generalised	Total
Focal lesion in MRI	37 (90.2 %)	4 (9.7 %)	41
Multifocal / Generalised lesions in MRI	0	51 (100%)	51
Fishers exact test: p – 0.000 Spearman correlation value - 0.39, p – 0.000			

Table :6 The association between locations of MRI findings were analysed against the clinical course of individual seizure episodes. Patients with multifocal lesions and generalised lesions were clumped together. There was significant association between (p-0.000) MRI lesions and the clinical course of seizure episode. Patients with focal lesions have significantly higher incidence of focal seizures and patients with multifocal / generalised lesions have higher incidence of generalised seizures. Spearman correlation was 0.39 with p – 0.000 suggesting positive correlation.

Table :7 MRI Vs EEG findings:

	Focal EEG findings	Multifocal or Generalised EEG findings	Total
Focal lesion in MRI	17 (89.4 %)	2 (10.6 %)	19
Multifocal / Generalised lesions in MRI	3 (12 %)	22 (88 %)	25
Total	20	24	44
Fishers exact test: p-0.000 Spearman correlation value – 0.848; p-0.000			

Table :7Among the patients with MRI findings, 44 patients had EEG data. Association between MRI findings and EEG findings were analysed. There was significant association between focal changes in MRI and focal EEG abnormalities (p-0.000). Similarly multifocal / generalised MRI findings were associated with multifocal / generalised EEG abnormalities.Spearman correlation also confirmed the positive correlation between MRI and EEG findings (p-0.000).

Discussion

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In our study 216 patients were included and 92 patients (42.6%) had structural lesions in MRI. Among them 41 had focal lesions and 51 had generalised or multifocal lesions. Localisation of MRI finding correlated well with onset of seizures and clinical course of seizures. MRI localisation also correlated with EEG localisation. Patients with MRI had significant higher number of antiepileptic drugs when compared to patients without MRI findings. However no significant correlation was observed between MRI localisation and pharmacotherapy.Epilepsy is one of the most common neurological illnesses encountered in paediatric population.[8] The burden of epilepsy is on increasing trend especially in developing countries. Epilepsy disorder in pediatric population has significant impact in health care expenditure. Patients are prescribed multiple antiepileptics and the side effects of those drugs like hepato toxicity, behavioural disturbances, haematological and electrolyte changes also possess significant impact in patient management. Some patients are refractory to medical therapy. These kinds of patients may need non pharmacological therapy like epilepsy surgery.[9] Identification of this group of patients and evaluation for structural lesions forms the crux of epilepsy management in refractory cases.Various modalities like CT imaging, MRI, EEG, video EEG, functional MRI, PET and SPECT scans have been used to identify structural lesions in patients with epilepsy. All the modalities have different sensitivity and specificity and different cost effectiveness in identifying structural lesions in epilepsy patients. Though MRI is costlier than CT imaging it has higher resolution. However the duration of MRI is longer mandating anaesthesia intervention and it is contraindicated in patients with metallic implants. Apart from these drawbacks, the incidence of MRI findings also varies among geographical regions.[10] Our study was planned to assess the utility of MRI in identifying structural lesions in a sample of south Indian population which was not available in current literature.In our study 42.6% of the population (n=92) had structural lesions in MRI. Studies from developed countries have mentioned the incidence of structural lesions in MRI in epilepsy patients ranging from 15 – 23%. However in developing countries like Latin America and Africa the incidence is quoted as much as 58%.[11]In a study from northern Indian states it was quoted that the MRI findings were seen in approximately 35% of population. As the primary aim of the study was not identifying MRI lesions the exact incidence was not quoted. In our study we found MRI lesions in 42.6% of the population which was higher than from developed countries and comparable to developing countries.[12]In those patients who had structural lesion in MRI, 44% of the population had focal lesions and 56% of the population had multifocal or generalised lesions. Among focal lesions focal gliosis constituted 36.5 %. In our population 12 patients (29.2%) had lesions suggestive of tuberculoma and 3 patients (7.3 %) had lesions suggestive of Neurocysticercosis. Studies have shown higher incidence of infectious aetiology in tropical and developing countries.[13] Our study results also closely correlates with available literatures.Among the generalised lesions diffuse cerebral atrophy was common finding (n=17; 33.3%) in our population. Diffuse gliosis, periventricular leukomalacia and basal ganglia hyperintensity were the next common findings. Periventricular lekomalacia was commonly associated with history of hypoxic ischemic encephalopathy. Basal ganglia hyperintensity was commonly associated with mitochondrial encephalopathy in our population.There was no significant difference in demographic parameters like age and gender in patients with and without MRI findings. [14]This suggests that there are no age or gender predilections to have structural lesions in MRI in patients with epilepsy. MRI findings were positively correlated with onset of seizures. Currently used classification of epilepsy is based on the onset of any seizure episode. In our study focal lesions in MRI were associated with focal onset of seizures and multifocal or generalised lesions were associated with generalised onset of seizures. This shows that MRI is useful in clinical classification of seizures even if history is doubtful.[15] In our study MRI findings were positively correlated with clinical course of seizure episodes. Patients with well defined focal lesions predominantly had focal seizures. On the other hand in patients with multifocal or generalised lesions the seizure progressed to generalised episode. This shows that MRI is useful in predicting clinical course of seizure episode.In our study 44 patients had MRI lesions and EEG together. Analysis showed that localisation of MRI findings (Focal / Generalised)

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correlated well with abnormal EEG pattern (Focal / Generalised). [16]This shows that MRI is also a good predictor of EEG findings in epilepsy patients. Various studies have shown that MRI has good correlation with EEG findings and they are useful adjuncts in evaluating a patient for epilepsy disorders. The correlation between clinical presentations (Video EEG), inter-ictal EEG localisation and MRI are now mandatory for evaluating a patient for surgical management of epilepsy.Commonly used drugs in our out-patient clinics were Phenytoin, Carbamazepine, sodium valproate, phenobarbitone and leviteracetam. In our study we found that in patients with structural lesions in MRI needed significantly higher number of antiepileptic drugs than patients without MRI lesions.[17] In patients with MRI lesions significant number of patients were prescribed 3 or 4 drugs. Studies have shown that in patients with multiple anti-epileptics the drug intolerance and drug resistance is higher and these patients may be considered for non pharmacological treatment modalities.[18] In our study it is demonstrated that MRI is correlating with pharmacotherapy and thus helping in planning treatment modalities. Our study also showed that there is no difference in pharmacotherapy between patients with focal or generalised MRI findings.[19,20]

Conclusion

MRI findings in our study population correlated well with the type of seizures at onset and the clinical course of seizures, focal lesions tending to have focal seizures at onset and throughout the clinical course.MRI findings correlated well with EEG lateralisation.Patients with definitive structural lesions were quite refractory to medical therapy and were on multiple drugs than those with normal MRI findings. Among the south Indian population, common aetiologies for epilepsy were hypoxic ischemic sequelae followed by tuberculosis. Mitochondrial disorders were also on increasing trend when compared to neuronal migration defects and other malformations as seen in developed countries.

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