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Role of MR imaging in the evaluation of etiology of seizures: an Observational Cross Sectional Study

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ABSTRACT

Background: Around 50 million people are living with epilepsy. Upto 70% of them can live seizure free life when diagnosed and treated correctly. Magnetic resonance imaging (MRI) has emerged as diagnostically valuable tool for localizing the epileptogenic focus preoperatively. Hence, this study was conducted with aim to assess utility of MRI in seizure patients for detection of etiologies.

Materials and methods: This was a cross sectional observational study performed in 152 patients with seizure. The study conducted from October 2017 to October 2019. Patients satisfying inclusion and exclusion criteria and who gave written informed consent were enrolled in the study. Data was expressed as percentage and mean ± SD. Chi square test was used to analyze significance of difference between frequency distribution. Sensitivity, specificity, negative predictive value and positive predictive value was calculated using standard formulae. P value <0.05 was considered as statistically significant.

Results: Majority 29 (19.1%) patients were </=5 years followed by 25 (16.4%) patients of 51-60 years of age. MRI findings were abnormal in 97(63.81%) patients. When diagnostic significance of MRI was compiled using EEG as baseline, sensitivity was 78.68%, specificity was 45.05%, positive predictive value (PPV) was 64.47% and negative predictive value (NPV) was 35.52%.

Conclusion: MRI provides an explanation for cause of seizures and explain about the need for chronic anticonvulsant therapy or possible surgical resection. Diagnostic significance of MRI was better than that of EEG for evaluating patients with seizures..

Keywords: Electroencephalogram, Magnetic resonance imaging, Seizures.

INTRODUCTION

A seizure is a paroxysmal alteration in the neurologic function which results from abnormal and excessive neuronal electrical activity. Epilepsy is a chronic condition that is characterized by recurrent seizures which are unprovoked by an acute systemic or neurologic insult.[1] Epilepsy is second most common and regularly encountered neurological condition enforcing heavy burden on individuals, families and healthcare systems.[2]

Epilepsy is a chief public health problem in developing nations like India. In India, approximately 10 million people are suffering with epilepsy and the prevalence is dominating in the rural (1.9%) as compared with the urban population (0.6%). Incidence rates of epilepsy are around 60 per 1, 00,000 per year in developing countries as compared to around 24-53 per 1, 00,000 in developed countries. Worldwide, China and India, together consist of about 20% of epileptics.[3]

Many neuroradiological investigations can be used to diagnose and find out the etiology of the lesion in epilepsy which include x-ray of skull,

pneumocephalography, carotid angiography, Cerebrospinal fluid (CSF) examination, Electroencephalogram (EEG), Computed tomography (CT) and MRI.[4] MRI has emerged as diagnostically valuable and most important tool for localizing the epileptogenic focus preoperatively due toits excellent soft tissue contrast that allows thorough interpretation of anatomy, freedom from beam-hardening artifact in basal brain which happen with CT and the capacity for multiplanarimaging.[5]

The evaluation of seizures is a common indication for MRI.[6] Specific MRI technique used is to be determined by the specific type of seizure of the patient. New-onset seizures in an adult need the acquisition of routine T1- and T2-weighted images along with gadolinium-enhanced images.[1]

The role of MRI in epilepsy has been assessed through research in diverse contexts such as relation of seizure recurrence in patients taking anti-epileptic drugs if there was an associated lesion detected on MRI.[7] According to the National Institute of Health and Clinical Excellence (NICE) guidelines, MRI of the brain must be the investigation of choice in patients with epilepsy (children and adults) to screen for any structural abnormalities.[8]

Electroencephalographic (EEG) indicates the function of forebrain and is useful in diagnosing epilepsy, defining type of seizure disorder and the epileptogenic zone. The association of EEG and MRI studies is beneficial to decide whether the functional epileptic focus is same as the structural one.[9]

In a cross sectional study done by **Wieshmann**,[10] an abnormality was found in 49% of patients having focal epilepsy who had a standard MRI scan and in 72% of patients who had a seizure protocol MRI scan. An MRI protocol for seizures must comprise at least one sequence with coronal T1 weighted thin slices (slice thickness 1 mm to 2 mm).[10] **King et al.**[11] from their study recommended that the assessment of older children and adults with first onset seizures should have a detailed clinical assessment with early EEG and MRI for all patients except those in whom idiopathic generalized epilepsy is confirmed on their EEG or those with benign rolandic epilepsy.[11]

The primary role of a radiologist is to evaluate for the structural etiology for the patient's epilepsy.[12]In literature, very few studies are available stating role of MRI in evaluating the etiology of seizures as well as role of EEG in evaluating the cause of seizures in MR idiopathic patients. Hence, this study was planned with the following aims and objectives.

AIMS AND OBJECTIVES

The aim of the present study was to assess utility of MR imaging in seizure patients for detection of etiologies. The objectives of this study were to evaluate assessment of MRI and EEG in MR idiopathic patients and to identify medically and surgically treatable causes of seizure and aid in their timely management.

MATERIALS AND METHODS

This was a cross sectional observational study performed in 152 patients with seizure in Department of Radio diagnosis of NKP Salve institute of medical sciences, Nagpur. The study was carried out after obtaining approval of institutional ethics committee (IEC) from October 2017 to October 2019. Patients satisfying the following inclusion and exclusion criteria and willing to participate in this study were enrolled in the study.

Inclusion criteria: All patients with seizure who are referred to department of Radio diagnosis and willing to undergo MRI brain during the study period.

***Exclusion criteria*:** Patients with claustrophobia, with pacemakers and metallic prosthesis. Written informed consent was taken from every patient after explaining the study procedure in detail.

Procedure

A detailed history was taken and clinical examination was done. The points noted were duration of illness, type of seizures, any associated illness. Detailed clinical and neurological examination was done to find any neurological deficit. Based on the history and examination, a clinicoetiological diagnosis was made.

The procedure was briefly explained to the patient. Evaluation was done with the help of 1.5 tesla MRI machine.

Technique of examination: All patients were screened before entry into the MRI scanning room for ferromagnetic objects, cardiac pacemakers,

Volume 2, Issue 6; November-December 2019; Page No.361-369

aneurysmclips etc. Patients were examined in the supine position on the MRI machine after proper positioning, and immobilization of the head was obtained. The head coil was used for the scan. Initial topogram of the head was obtained and sequences were planned according to the MRI seizure protocol. MR imaging 16 channels GE 1.5 Tesla HDXT, Version 23.0.

Imaging protocol:[1]

The following sequences were used to evaluate seizure.

A dedicated head coil is used with a field of view ~22 – 24 cm.

A slice thickness of 3mm is used with an inter-slice gap of 0.6mm. The matrix size used is 512x 256.

Sequences used:

- Axial and sagittal T1W for cortical thickness and the interface between grey and white matter.
- Axial and coronal T2W/ FLAIR for cortical and sub cortical hyperintensities on the FLAIR, which can be very subtle.
- Axial DWI/ADC sequences to look for diffusion restriction in vascular compromise.
- Axial T2*/ SWI for hemoglobin breakdown products/ calcifications.
- Axial and coronal gradient echo sequences.
- Coronal T1W sequences angled perpendicular to temporal lobes in suspected temporal lobe pathologies.
- Axial T1 post contrast sequences.
- MR spectroscopy

As a precautionary measure, resuscitation apparatus and emergency drugs were kept ready. The scans were studied in detail on monitor and finally films were taken for permanent record. MRI findings were recorded in all patients as per the proforma. Every effort was made to make sure of high quality scans and to avoid artifacts. Also, all the patients underwent EEG to locate the epileptogenic focus.

Clinical data and findings of all patients were maintained in specified Performa.

At the end of study all the proformas were evaluated in details and observations were analyzed statistically.

Statistical analysis: Data was expressed as percentage and mean ± SD. Student's paired t test was used to assess the significance of difference between repeated means. Fischer's exact test or Chi square test was used to analyze the significance of difference between frequency distribution of the data. Sensitivity, specificity, negative predictive value and positive predictive value was calculated using standard formulae. P value <0.05 was considered as statistically significant. SPSS© for windows™ Vs 17, IBM™ Corp NY and Microsoft excel™ 2007, Microsoft® Inc USA was used perform the statistical analysis.

OBSERVATIONS AND RESULTS

In the present study, total 152 patients were distributed into different groups according to their age. 29 (19.1%) patients were </=5 years, 25 (16.4%) patients were 51-60 years, 17 (11.2%) patients were >60 years which was followed by patients in the age group 16-20 years and 21-25 years, each with 16 (10.5%) patients. 14 (9.2%) patients were 31-40 years, 9 (5.9%) patients each were present in 6-10 years and 41-50 years group. 6 (3.9%) patients were in 11-15 years group. Male predominance was seen with 84 (55.3%) males and 68 (44.7%) females.

Out of 152 patients in total, 57 (37.5%) patients were students while 22 (14.5%) patients were retired. For 20 (13.2%) patients occupation status was not available. 15 (9.9%) patients were farmers while, 14 (9.2%) patients were housewives. This was followed by service personnels with 11 (7.2%) patients, unskilled labourers with 3 (2%) patients and executives with 2 (1.3%) patients.

The mean BMI of study patients was 21.46 ±4.47. 93 (61.2%) patients were found to be normal while 25 (16.4%) patients were found to be overweight. This was followed by 22 (14.5%) patients in obese I category and 7 (4.6%) patients in underweight category. Only 5 (3.3%) patients were found to be in obese II category.

Volume 2, Issue 6; November-December 2019; Page No.361-369

The distribution of type of seizure noted was as depicted in Table 1.

Type of seizure	Frequency	Percent
Absence	2	1.3
Complex partial	7	4.6
Focal	12	7.9
Generalised tonic clonic	74	48.7
Simple febrile	14	9.2
Tonic	1	.7
Unclassified	42	27.6
Total	152	100.0

Table 1: Type of seizure involve in study patients

In this study number of seizures at presentation was noted. In 86 (56.6%) patients number of seizures was found to be 1 while, in 37 (24.3%) patients 2 seizure episodes were noted. This was followed by 4 seizures in 6 (3.9%) patients and no seizures in 2 (1.3%) patients. 6 and 12 seizures at presentation were noted in 1 (0.7%) patient each.

In majority 142 (93.4%) of patients non neurological problems were absent. Back pain, breathlessness and vomiting were noted in 2 (1.3%) patients each. While in 1 (0.7%) patient each CKD, depression, fever and hypoglycaemia was seen.

MRI findings in study patients were as stated in Figure 1 and EEG findings in study patients were as shown in Figure 2. Association of EEG findings with MRI findings was as depicted in table 2.

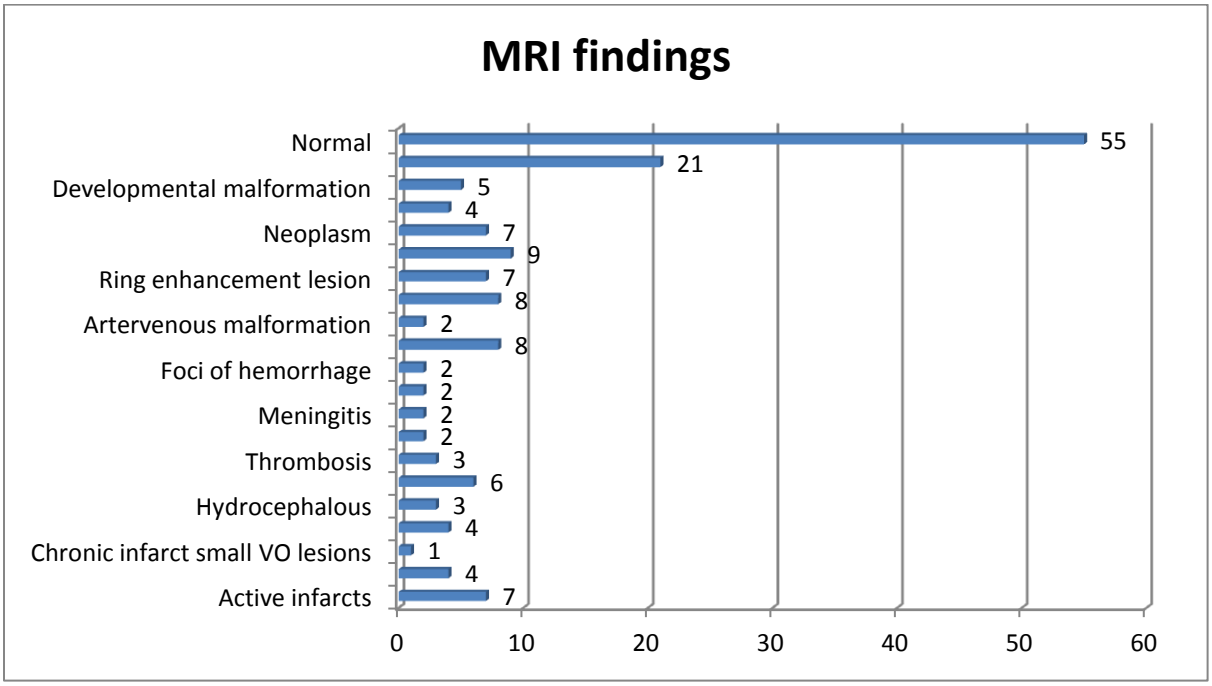

Figure 1: MRI findings in study patients

Volume 2, Issue 6; November-December 2019; Page No.361-369

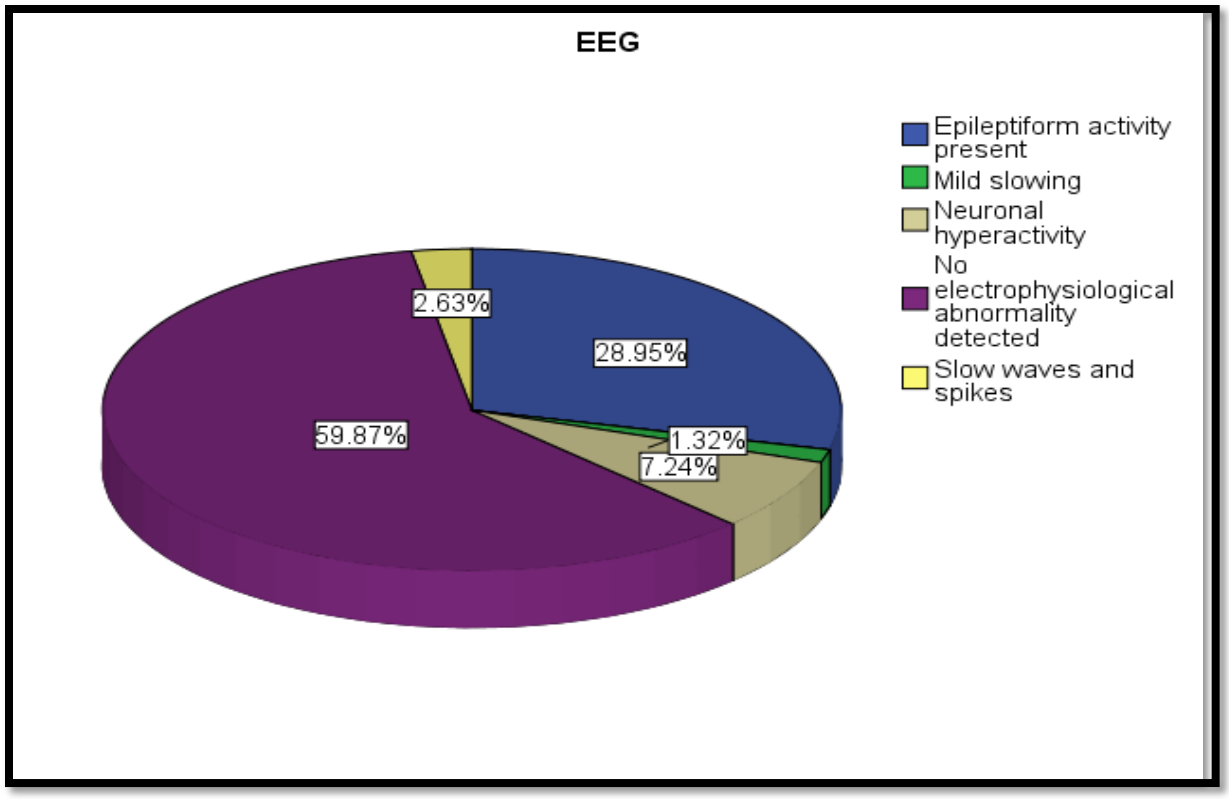

Figure 2: EEG findings in study subjects

		EEG Findings		Total
		A	N	
MRI Findings	A	48 78.7%	50 54.9%	98 64.5%
	N	13 21.3%	41 45.1%	54 35.5%
Total		61 100%	91 100%	152 100.0%

A- Abnormal, N- Normal

Table 2: Association of EEG findings with MRI findings

Significant difference was noted between the observations on these two mode of investigations.(P<0.05) When diagnostic significance of MRI was compiled using EEG as baseline, sensitivity was 78.68%, specificity was 45.05%, positive predictive value (PPV) was 64.47% and negative predictive value (NPV) was 35.52%.

Volume 2, Issue 6; November-December 2019; Page No.361-369

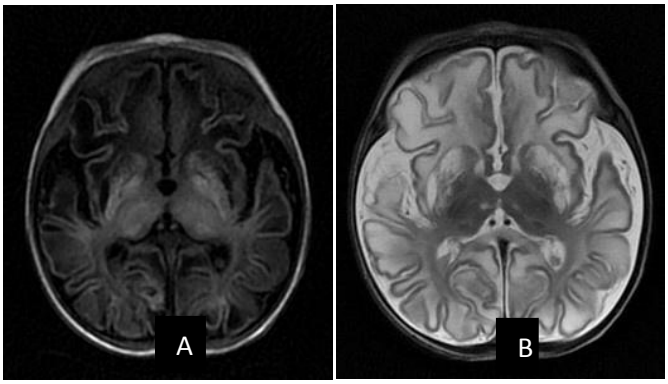

Figure 3 (A & B) : Axial T2W flair and T2 WI image shows altered signal intensities noted in deep grey matter nuclei involving bilateral thalami and few peripheral cystic changes in bilateral fronto-parietal region suggestive of sequelae of hypoxic ischemic encephalopathy.

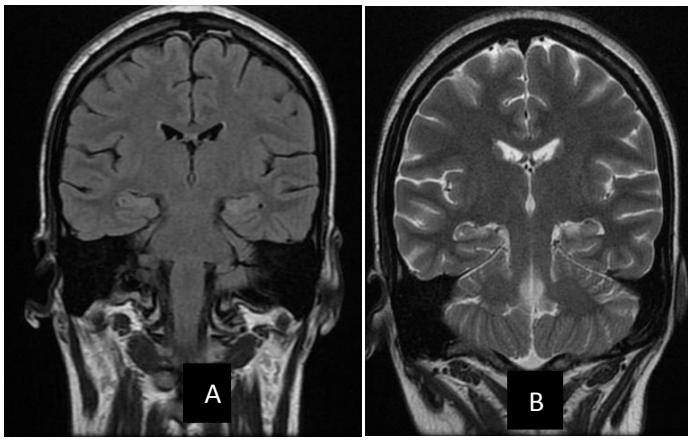

Figure 4 (A & B): COR T2W and T2 Flair image shows bilateral symmetrical altered areas of signal intensities in temporal lobe appearing hyperintense on T2 and FLAIR possibly suggestive of Mesial temporal sclerosis.

DISCUSSION

MRI has rationalized the neuroimaging and offers the best method of non-invasive assessment of structure of the brain. The spectrum of MRI in patients diagnosed with seizure range from nearly a normal scan to a scan presenting the culprit lesion. MRI is the critical component of pre-operative evaluation because, the type of surgery and its outcome is determined by the cause as well as location of the epileptogenic foci. MRI of brain is considered as the investigation of choice in epilepsy in children as well as adults for identifying structural abnormalities. The reason being, superior soft tissue contrast, multiplanar imaging capability and lack of beam hardening artefacts which are helpful in demarcating discrete lesions such as mesial temporal sclerosis (MTS), hypothalamic hamartoma or focal cortical dysplasia which can pave the way to surgery in cases of refractory epilepsy.[3]

In the present study, majority of the patients were </=5 years age group 29(19.1%) followed by 25(16.4%) patients in the age group of 51 to 60 years. The similar findings were reported by **Ponnatapura et al**.[13] and **Hakami et al.**[14]Male predominance shown in this study was consistent with study by **Patel et al.,**[3]male predominance was seen with 94 (62.67%) males and 56 (37.33%) females. Also, in a study by **Desai et al.,**[1] including patients with clinical history of new onset seizures, males were (62.8%) and females were (37.2%).

In the present study, mean BMI was 21.46 ±4.47. The distribution of patinets according to BMI was supported in a study by **Gao et al.,**[15]in patients with seizures which concluded that the incidence of seizures was higher in the extremely obese and

Volume 2, Issue 6; November-December 2019; Page No.361-369

underweight patients than in the normal weight patients.

In our study, distribution of type of seizure was noted. Generalised tonic clonic seizure was observed in 74 (48.7%) patients and in 42 (27.6%) patients seizures were found to be unclassified. 14 (9.2%) patients were found with simple febrile and in 12 (7.9%) patients focal seizures were observed. This was followed by complex partial type in 7 (4.6%) patients, absence of seizures in 2 (1.3%) patients and tonic types in 1 (0.7%) patients. In accordance with our findings, in a study by **Desai et al.,**[1] 73.7% (n=121) patients presented with generalised tonic clonic seizures, 10.9% (n=18) patients presented with focal seizures, 9.1% (n=15)patients presented with complex partial seizures and 6.3% (n=10) patients presented with other varieties such as absence seizures (n=2), myoclonic jerks (n=3), postpartum seizures (n=2) and status epilepticus (n=3).

In this study, MRI findings were abnormal in 97(63.81%) patients, rest of patients 55(36.18%) were with normal MRI findings. Out of abnormal MRI findings noted, atrophy was seen in 9(5.9%) patients followed by granuloma and edema was seen in 8 (5.26%) patients each. 7(4.61%) patients each had active infarcts, Ring enhancement lesion and neoplasm. 6(3.95%) patients showed haemorrhage and 5(3.29%) patients showed developmental malformations on MRI. 4(2.63%) patients each revealed chronic infarct, cystic encephalomalacia and medial temporal sclerosis (MTS) on MRI. 3(1.97%) patients each showed hydrocephalus and thrombosis. Two (1.32%) patients each showed Hypoxic injury, meningitis, encephalitis, foci of haemorrhage and arteriovenous malformations whereas only 1(0.66%) patient showed chronic ischemic small vessel disease. Other abnormal MRI findings were noted in 25(16.44%) patients. This was consistent with the study by **Patel et al.,**[3] in which the abnormal MRI findings were seen in 93 (62%) patients. MRI revealed acute infarct in 11 (7.3%), chronic infarct in 4 (2.7%), cystic encephalomalacia in 15 (10%), chronic small vessel disease in 25 (16.7 %), tumours in 13 (8.7%), hydrocephalous in 4 (2.7 %), developmental malformations in 1 (0.7%), infective in 15 (10%), demyelinating lesions in 9 (6%), vascular malformations in 3 (2%), haemorrhage in 7 (4.7 %), thrombosis in 5 (3.3 %), MTS in 5 (3.3 %), atrophy in 20 (13.3%), oedema in 11 (7.3 %) and hypoxic injury in 5 (3.3 %) patients. Also, in a study by **Mercy NN.,**[16]in patients of epilepsy, 61.6% of the MRI scans were abnormal. The MRI findings were diverse including MTS in (10.6%), infarction in (9.3%), tumours in (8.6%), infection in (7.3%) and atrophy in (7.3%).

However, according to study by **Mohammadi et al.,**[17]only (29.27%) had abnormality on MRI. The most common imaging findings were gliosis in 10 (10.4%), dysmyelination 6 (7%), hemorrhage in 5 (5.2%) and brain dysgenesis in two (2%). In contrast to our findings, study by **Hakami et al.**[14] **and Nguyen et al.,**[18] showed prevalence of MTS of 9 % and 17 % respectively, however, these studies were having much bigger sample size as compared to our study. In a study by **Nguyen et al.,**[18]the prevelance of MRI findings was more as compared to our study which may be probably due to a much larger sample size as compared with our study.

In our study, in 91 (59.9%) patients no electrophysiological abnormality was detected but 61 (40.1%) patients showed abnormal EEG findings. Epileptiform activity was noted in 44 (28.9%) patients and neural hyperactivity was noted in 11 (7.2%) patients. This was followed by slow waves and spikes in 4 (2.6%) patients and mild slowing in 2 (1.3%) patients. Similarly, in a study by **Ponnatapura et al.,**[13] out of 126 patients, 39 (31%) patients showed abnormal recordings and 87 (69%) showed normal recordings on EEG. Out of the 39 abnormal recordings, 12 (31%) patients showed generalized slowing and 18 (46%) patients showed epileptic discharges on EEG.

In the present study, 98(64.5%) patients and 61 (40.1%) patients had abnormal MRI and abnormal EEG findings respectively. 48 (31.6%) patients had an abnormality on both MRI and EEG showing that abnormal MRI and EEG were concordant in 31.6% of patients. When association of EEG findings with MRI findings was assessed, statistically significant difference was noted between distributions of observations on these two mode of investigations suggesting that EEG findings are not good indicators of MRI findings. Further, when diagnostic significance of MRI was compiled using EEG as baseline, where sensitivity was 78.68%, specificity was 45.05%, PPV was 64.47% and NPV was 35.52%. Similarly, in a study by **Ponnatpura et al.,**[13]

Volume 2, Issue 6; November-December 2019; Page No.361-369

there were 22 patients (18%) with an abnormality on both MRI and EEG showing that abnormal MRI and EEG were concordant in 18% of patients. They also revealed that the diagnostic yield of MRI was high, detecting epileptogenic lesion in approximately half of the patients with epileptic seizures. In contrast to our study, **Najafi et al**.,[19] in their study which was conducted to evaluate the MRI and EEG findings in patients with epilepsy reported that 25.6% of studied patients had abnormal MRI and 62.3% had abnormal EEG.

The differences between study findings may be due to differences in study design, the technology used, the patient population studied and the range of MRI abnormalities included as abnormal. The duration of epilepsy is also significantly associated with abnormality on MRI, indicating that longer duration of epilepsy could be a predictor of abnormal MRI.[19]

***Limitation*:** It was a single centre study. More recent advances like MR spectroscopy, receptor PET, and magnetic source imaging may be helpful in understanding the biomarkers involved in the epileptogenic process and thereby aid in localising the epileptogenic focus in cases where routine MRI is normal.

CONCLUSION

MRI has a pivotal role in the evaluation of etiologies of seizures. MRI is highly sensitive and specific in identifying the underlying pathology in seizures. MRI provides an explanation for cause of seizures and explains about the need for chronic anticonvulsant therapy or possible surgical resection. Diagnostic significance of MRI was better than that of EEG for evaluating patients with seizures. However, in patients having a normal MRI of brain, further evaluation with EEG correlation can be helpful in identifying epileptic focus.

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Volume 2, Issue 6; November-December 2019; Page No.361-369

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Volume 2, Issue 6; November-December 2019; Page No.361-369