

Evaluation Of Non Febrile Seizure Disorder On MRI With Correlation With Seizure Type And EEG Records In A Tertiary Care Teaching Hospital

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Abstract

Objective— This study was done to assess the spectrum of pathology of non febrile seizure disorder on MRI, to correlate MRI findings with the seizure type and EEG records wherever available and assessment of relevance of observed findings.

Methods: A retrospective hospital based study was done of 321 patients who underwent brain MRI for seizure disorder with exclusion of febrile conditions, recent trauma and metabolic conditions from the study. The MRI findings were interpreted independently and subsequently correlated with clinical history and EEG findings wherever available from patients' records.

Results- Out of the 321 patients included in the study, 191 patients (59.5%) were male and 130 patients (40.5%) were female. 227(72%) patients were under 30 years of age out of which 102 (31.8%) were in 11-20 years age group . Interictal awake scalp EEG findings were available in 155(48.2%) cases. In the 219 (68.2%) cases with abnormal MRI findings granulosomatous lesion was the most common abnormality in 91 (28.3%) cases, followed by focal gliotic/encephalomalacic changes in 32 (10%) cases, tumors in 20 (6.2%) cases, periventricular leukomalacia/ hypoxic ischemic encephalopathy in 14 (4.4%) cases, diffuse significant brain atrophy in (4.1%) cases, congenital/developmental anomalies in 11(3.4%) cases, mesial temporal sclerosis in 10 (3.1%) cases and miscellaneous other conditions in 21 (6.5%) cases. Most common seizure type was generalized tonic-clonic (43.9% cases), followed by generalized tonic or clonic (19%), complex partial (11.2%), simple partial (10 %), partial seizures with secondary generalization (8.7%), with rest of the seizure types comprising less than 10% of the cases. There was a very high rate of abnormality detection on MRI with atypical absence, partial or partial seizures with secondary generalization with most of these patients having EEG records suggestive of seizure activity. Patients presenting with primary generalized tonic-clonic, tonic or clonic and absence seizures had relatively lower rate of abnormality detection on MRI and EEG.

Conclusion- This study shows an overwhelming predominance of children, adolescents and young adults in patients being investigated for seizure disorder with primary generalized seizures being the most common presentation. CNS granulosomatous pathology (predominantly NCC) and gliotic/encephalomalacic foci were the two most common abnormalities detected on MRI. Prior knowledge of seizure type and EEG records can be helpful factors in increasing diagnostic efficacy of MRI and avoiding unnecessary imaging.

INTRODUCTION

Epilepsy and seizure disorder are a significant health problem in developing countries around the world. The advances made in the field of neuroimaging particularly magnetic resonance imaging (MRI) have fortunately revolutionized the evaluation and management of epilepsy and seizure disorders.^{1,2} This retrospective hospital based study was done in a semiurban tertiary healthcare setup in

Northern India to assess the spectrum of pathology of non febrile seizure disorder via MRI and to correlate MRI findings with the symptomatology and EEG wherever available as well as assessment of relevance of observed findings.

A seizure is a paroxysmal alteration in neurologic function resulting from abnormal excessive neuronal electrical

activity. The pathophysiologic basis of seizures is loss of normal regulation of neuronal excitation and inhibition, resulting in a state of relative hyperexcitability.³ Epilepsy is a chronic condition characterized by recurrent seizures unprovoked by an acute systemic or neurologic insult; the term itself does not indicate a specific underlying pathology.^{3,4}

The most widely used classification of epileptic seizures is the International League Against Epilepsy (ILAE) classification (Table 1), which is principally based on the clinical seizure type and interictal electroencephalography (EEG) findings.⁵

Table 1
Classification of Seizures

Table 1 Classification of Seizures ⁵	
1. Partial seizures	
a.	Simple partial seizures (with motor, sensory, autonomic, or psychic signs)
b.	Complex partial seizures
c.	Partial seizures with secondary generalization
2. Primarily generalized seizures	
a.	Absence (petit mal)
b.	Tonic-clonic (grand mal)
c.	Tonic
d.	Atonic
e.	Myoclonic
3. Unclassified seizures	
a.	Neonatal seizures
b.	Infantile spasms

Role of MRI in evaluation of seizures/epilepsy

MRI is the imaging procedure of choice for the investigation of patients with epilepsy.² Magnetic resonance imaging has been shown to be superior to CT for the detection of cerebral lesions associated with epilepsy. However, the disadvantages of MRI are its unavailability for larger number of patients, higher cost, and the requirement for longer time periods for scanning. The sensitivity of MRI in detecting abnormalities in patients with epilepsy is in part associated with pathologies underlying epilepsy, and also by MRI techniques and the experience of interpreting radiologists. A typical clinical scanning protocol for a patient with seizure disorder includes T1 -weighted imaging, T2-weighted imaging, fluid-attenuated inversion recovery (FLAIR) imaging, and 3D volume acquisition sequences.⁶ T1-weighted (short repetition time (TR) and echo time (TE) are commonly used for defining the brain anatomy and can be helpful in identifying hemorrhage, fat containing and

sometimes calcified lesions. In T2-weighted images (long TR, long TE), certain types of brain pathologies are discernable. On FLAIR images, the CSF appears dark, which helps to identify lesions with long T2-relaxation times. A high-resolution 3D volume acquisition provides a useful degree of T1-weighted contrast between grey and white matter, and helps greatly in the identification of subtle abnormalities, such as those associated with malformations of cortical development.⁷

Recently there has been increasing utilization of MR spectroscopy, tractography and functional MRI combined with quantitative EEG in the evaluation of seizure disorders/epilepsy.^{2,8} However these facilities are available in only few specialized centers in developing world and still under evaluation and development.

Role of EEG

National Institute for Clinical Excellence (NICE) guidelines for diagnosis and management of the epilepsies in adults and children recommend that an EEG should be performed to support a diagnosis of epilepsy in adults in whom the clinical history suggests the seizure is likely to be epileptic in origin. In children, EEG is recommended after the second or subsequent seizure.⁹

EEG helps determine seizure type and epilepsy syndrome in patients with epilepsy, and thereby choice of antiepileptic medication and prediction of prognosis. EEG findings contribute to the multi-axial diagnosis of epilepsy, in terms of whether the seizure disorder is focal or generalised, idiopathic or symptomatic, or part of a specific epilepsy syndrome. Routinely awake interictal scalp electrode EEG is performed with addition of sleep, hyperventilation and photic stimulation protocols to increase diagnostic yield.¹⁰

The absence of electrographic seizure activity does not exclude a seizure disorder, however, because simple or complex seizures may originate from a region of the cortex that is not within range of the scalp electrodes. Since seizures are commonly infrequent and unpredictable, it is often not possible to obtain the EEG during a clinical event and interictal EEG in such cases may be normal. Use of video-EEG (VEEG) telemetry units for hospitalized patients or the portable equipment to record the EEG continuously on cassettes for 24 hours in ambulatory patients can be done in such cases. In particular, video-EEG telemetry is now a routine approach for the accurate diagnosis of epilepsy in patients with poorly characterized events or seizures that are

difficult to control.⁴

PATIENTS AND METHODS

This hospital based retrospective study was conducted in Department of Radiodiagnosis and Imaging and interventional Radiology, Subharti Medical College and affiliated CSS Hospital, Meerut. A total of 321 patients of all age groups who underwent MRI of brain for seizure disorder from November 2010 till October 2012 were included. Scanning protocol included Axial T1, T2, T2Flair, Diffusionweighted, GRE sequences along with Coronal T2, FLAIR and 3D T1 spoiled gradient sequences with additional thin section Fiesta C and post gadolinium T1 sequences wherever applicable done on 1.5T GE Signa HDEMRI scanner. Cases of seizures in setting of fever, recent trauma and metabolic disorders were excluded. The MRI findings were interpreted independently and subsequently correlated with clinical history and interictal awake scalp EEG findings(available in 155 cases) from patients

RESULTS

Out of the 321 patients included in the study, 191 patients (59.5%) were male and 130 patients (40.5%) were female, male to female ratio being 1.5:1. 72% of the patients belonged to the age group of less than 30 years while 24% of the patients were in the 31-60 years age group. The age group wise distribution of patients is given in the table no.2.

Table 2

Age group in years	Cases (%)
0-10	53 (16.5%)
11-20	102 (31.8%)
21-30	72 (22.4%)
31-40	44 (13.7%)
41-50	19 (5.9%)
51-60	14 (4.3%)
61-70	13 (4%)
71-80	2 (0.6%)
81 and above	2 (0.6%)
Total	321

In the present study, patients with generalized seizures outnumbered partial seizures. Most common seizure type was generalized tonic-clonic (43.9% cases), followed by generalized tonic or clonic (19% cases), complex partial (11.2%), simple partial (10 % cases), partial seizures with secondary generalization (8.7% cases), with rest of the seizure types comprising less than 10% of the cases (Table no.3).

Table 3

Type of seizure	No. of cases (%)	Abnormal MRI (%)	No. of EEG s/o seizure activity/ No. of EEG records available
Simple partial	32 (10%)	29 (90.6%)	10/16 (62.5%)
Complex partial	36 (11.2%)	30 (83.3%)	19/24 (79%)
Partial with secondary generalization	28 (8.7%)	28 (100%)	10/14 (71.4%)
Generalised Tonic-clonic	141 (43.9%)	98 (69.5%)	37/54 (68.5%)
Tonic or clonic	61 (19%)	24(39.3%)	15/36 (41.7%)
Atonic	2 (0.6%)	1(50%)	-
Myoclonic	4 (1.2%)	1 (25%)	-
Absence	6 (1.8%)	0 (0%)	2/4 (50%)
Atypical absence	7 (2.2%)	7 (100%)	5/6 (83.3%)
Unclassified	4 (1.2%)	1(25%)	-

In cases presenting with atypical absence, partial or partial seizures with secondary generalization there was a very high rate of abnormality detection on MRI with most of these patients having abnormal interictal awake EEG records suggestive of seizure activity. Patients presenting with primary generalized tonic-clonic, tonic or clonic and absence seizures had relatively lower rate of abnormality detection on MRI and EEG. This difference being statistically significant (p value < 0.05). There was strong positive correlation between MRI abnormality and abnormal seizure activity on EEG (Pearson correlation coefficient r = 0.83).

102 (31.8%) of the 321 patients in the study group had completely normal MRI findings Of the rest of the 219 (68.2%) cases with abnormal MRI findings granulosomatous lesionand focal gliotic/encephalomalacic changes were the two most common abnormalities seen in 38.3% cases (table no.4). Neurocysticercosis was the common granulosomatous lesion detected on MRI.

Table 4

Predominant MRI abnormality	No. of cases (%)
Granulomatous lesion	91 (28.3%)
NCC	65 (20.2%)
others	26 (8.1%)
Focal Gliotic/encephalomalacic changes	32 (10%)
Tumor	20 (6.2%)
Periventricular leukomalacia /HIE	14 (4.4%)
Atrophy	13 (4.1%)
Congenital/ developmental anomaly (Cortical dysplasia, grey matter heterotopia, TS, hemimegalencephaly, leukodystrophy etc)	11 (3.4%)
Mesial temporal sclerosis	10 (3.1%)
Cerebral venous thrombosis	5 (1.6%)
Posterior reversible encephalopathy (PRES)	2 (0.6%)
Misc. Incl:	21(6.5%)
Hydrocephalous	5 (1.6%)
Small vessel ischemic disease	5 (1.6%)
Non traumatic Intracranial bleed	3 (0.9%)
Vascular malformation	2 (0.6%)
SSPE	2 (0.6%)
Leptomeningeal cyst	1 (0.3%)
Neuroglial cyst	1 (0.3%)
Post ictal changes	1 (0.3%)
ADEM	1 (0.3%)
Total	219 /321(68.2%)

Granulomatous lesions were predominantly seen in patients less than 40 years of age and most frequently in 11-20 years age group, while focal gliotic/ encephalomalacic changes were most frequently observed in 11-30 years age with second peak in 51-70 years age groups. Tumors were most commonly seen in 30 years or older age group whereas periventricular leukomalacia/ HIE had presentation entirely in less than 30 years age group in patients with seizures. Congenital/developmental disorders as name implies had presentation in less than 30 years. Similarly MTS predominantly presented in less than 30 years age group. Miscellaneous conditions like vascular formations, ADEM, SSPE, hydrocephalous had presentations in younger age groups while intracranial bleed and cysts presented in more than 30 years age groups. (table no.5)

Table 5

Predominant MRI abnormality	Age group wise distribution								
	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81 & above
Granuloma	19	37	18	10	6	1	0	0	0
Focal Gliotic /encephalomalacic changes	3	6	7	4	3	3	6	0	0
Tumor	0	2	3	4	2	5	2	2	0
Periventricular leukomalacia /HIE	6	6	2	0	0	0	0	0	0
Atrophy	2	0	1	1	1	4	2	0	2
Congenital/ developmental anomaly	7	1	2	0	1	0	0	0	0
Mesial temporal sclerosis	1	4	3	1	1	0	0	0	0
Cerebral venous thrombosis	0	1	2	1	0	0	1	0	0
Posterior reversible encephalopathy (PRES)	0	0	2	0	0	0	0	0	0
Misc.	6	5	3	4	1	0	2	0	0

Figure 1

MRI Fiesta sequence showing degenerating neurocysticercosis with scolex within in the right frontal lobe

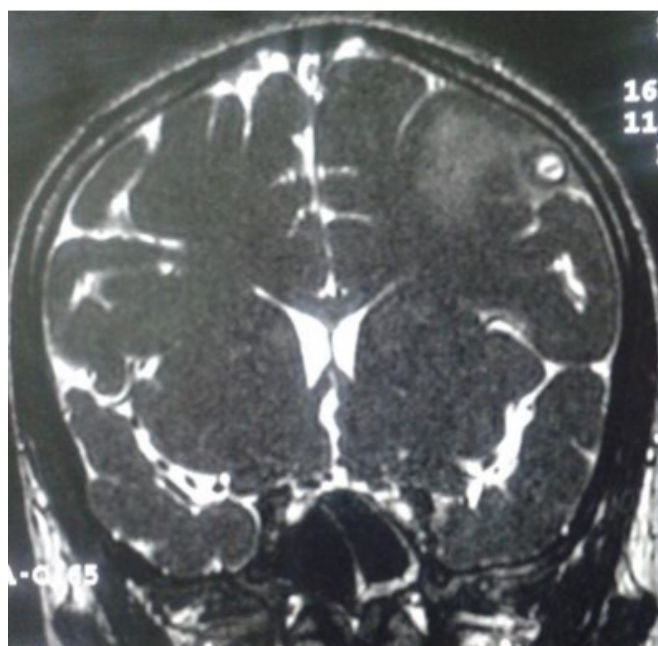


Figure 2

Cor T2 Flair Image showing focal cortical dysplasia in left superior frontal lobe

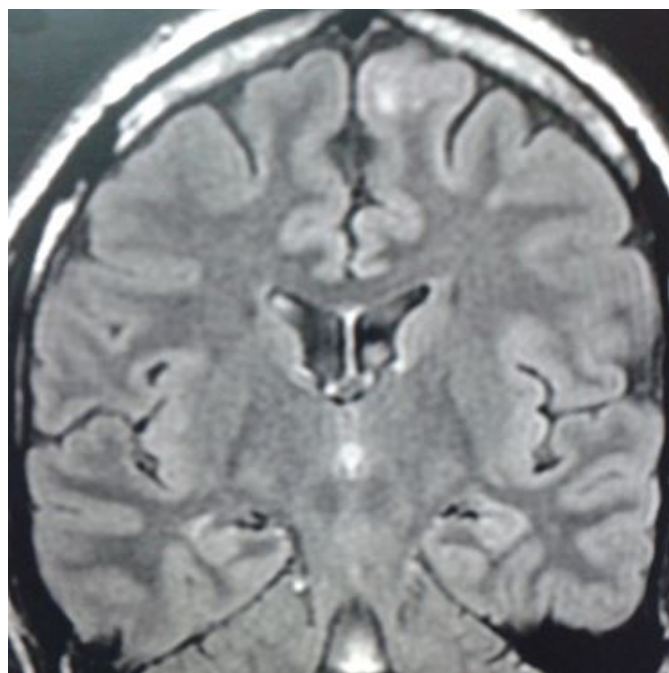


Figure 4

Axial T2 Flair image showing gliotic encephalomalacic changes in left high parietal lobe

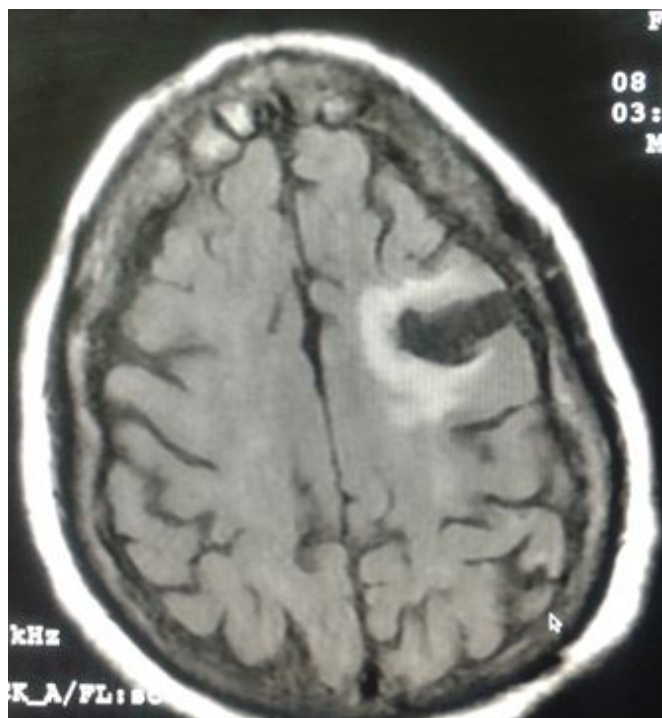


Figure 3

Axial T2W image showing changes of hypoxic ischemic encephalopathy



DISCUSSION

This retrospective study done in a semiurban tertiary care hospital reveals that majority (>70%) of patients being investigated for seizure disorder fall in the less than 30 years age group with maximum number of patients in the 11-20 years age group, which is in agreement with other studies done in Indian subcontinent^{11,12} and across Asia¹³ as well as sub Saharan Africa¹⁴ and southern American developing countries.^{15,16} This trend is different from that observed in developed countries with bimodal peaks in young children and elderly patients¹³ and declining trend in younger age group with increase in older patients.^{17,18}

Most common seizure pattern in our study was generalized tonic-clonic followed by generalized tonic or clonic seizures (62.9% cases). Localised/partial seizures and those with secondary generalization were observed in approximately thirty percent of the patients while rest of the seizure types described comprised less than ten percent of the patients. This trend of predominance of primary generalized epilepsy is in agreement with various other studies done in India^{11, 19-21} and other developing countries across Asia¹³ and sub Saharan Africa.¹⁴ In contrast Hart et al in UK²², Borges et al in Brazil²³ and Hauser et al in US²⁴ found predominance of partial seizures in their study populations.

The predominant abnormality detected on MRI in this study was granulomatous lesion followed by gliotic/encephalomalacic changes likely consequent to previous ischemic, infective or traumatic insults followed by tumors, perinatal insult (HIE) and atrophy. Likewise CNS infections/infestations, previous head injury, and perinatal insult have been found to be most common etiologies associated with seizures in various studies done in developing countries.^{13,14,25} Neurocysticercosis was overall the most common abnormality (20% cases) seen in our study group. Rajbhandari in Nepal²⁶, Garcia et al in Peru²⁷ and Medina et al in Mexico²⁸ have similarly found neurocysticercosis the major cause of epilepsy in their study populations.

Overall MRI detected abnormality in majority (68.2 %) of patients in this hospital based study. MRI in our study had a high rate of abnormality detection in case of partial seizures, partial seizures with secondary generalization and atypical absence seizures while it had somewhat limited utility in patients with primary generalized seizures. There was strong positive correlation between MRI and EEG findings i.e. abnormality detection on MRI was higher in patients with EEG records suggestive of seizure activity. This shows that MRI is likely to be diagnostic benefit in patients with partial, secondary generalized and atypical seizures or relevant EEG abnormalities while its diagnostic yield may be limited with other seizure types and normal EEG findings. These findings are of significance in developing world with limited healthcare resources and significant affected populations. Proper clinical characterization of seizure type and features and EEG prior to MRI can be of help in increasing the diagnostic efficacy and avoiding unnecessary imaging. Though this view is shared by limited literature,^{29,30,31,32} larger studies in general population are warranted.

CONCLUSION

This study shows an overwhelming predominance of children, adolescents and young adults in patients being investigated for seizure disorder with primary generalized seizures being the most common presentation. CNS granulomatous pathology (predominantly neurocysticercosis) and gliotic/encephalomalacic foci were the two most common abnormalities detected on MRI. Prior knowledge of seizure type and EEG records can be helpful factors in increasing diagnostic efficacy of MRI and avoiding unnecessary imaging.

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