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Role of CT and MR Imaging in Non Neoplastic Aetiologies of Seizure Disorder in 6-18 Yrs Age Group

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Original Research Article

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Abstract: Neuroimaging is one of the most important advances in the past decade in the management of seizure disorder. Neuroimaging has increased substantially the ability to plan medical, surgical therapy and to prognosticate the outcome of disorder and therapy. Neuroimaging help to determine whether seizure was provoked or unprovoked. Distinction between two types of epilepsy is a major determinant in selecting the antiepileptic medicine to treat the disorder. Present study was done to identify CNS lesion in patients with seizure whether it matches with seizure semiology. And to characterize the lesion and help to plan out whether medical or surgical modalities required. It was a hospital based cross sectional observational study. Age, sex, characterization of seizure including onset, time of attack ,provocative factors, first attack, total no of attacks, frequency of attack, status of consciousness, prodrome, aura, cerebellar symptoms, duration, post ictal phenomenon, history of drug intake, control of attack by drugs, family h/o of seizure, birth history were noted. In the present study 34.5% of children belong to 6-9 yrs age group followed by 27.6% of 16-18 yrs group. Aetiologies identified through imaging process in the present study were mainly normal (24.14%), mesial temporal sclerosis, congenital structural defect and infective (17.24%) each. Causes of congenital aetiologies of seizure identified through MRI imaging was mainly Dyke Davidoff Mason syn and Arachnoid cyst (22.22% each) followed by Sturge weber syndrome, Chiari-I malformation, septo-optic dysplasia, corpus callosum agenesis, pachygyria and porencephalic cyst (11.11% each). Determining whether focal lesion is the cause of seizure also helps in diagnosis of epilepsy syndromes of childhood. Neuroimaging is useful to determine whether early intervention is required or not as in cases of traumatic seizure, vascular aetiologies of seizure.

Keywords: Seizure disorders, Non-neoplastic aetiologies, MRI, CT imaging, Neuroimaging.

INTRODUCTION

Seizure (from the latin word sacire – "to take possession of") is most easily defined in physiological terms being the name for occasional, sudden, excessive, rapid and local discharge from gray matter [1]. Epileptic seizure can be defined as intermittent and stereotyped disturbances of consciousness, behaviour, emotion, motor function or sensation that on clinical ground believed to be result from cortical neural discharge [2]. Epilepsy can be defined as two or more

unprovoked seizure occurs at an interval of 24 hrs or more apart [3].

Although variety of factor influences the incidence and prevalence of seizure 5-10% of the population will have at least one seizure in their lifetime with the highest incidence of occurring in the childhood and late adulthood [4].

Using the definition of epilepsy as two or more unprovoked seizure, the incidence of epilepsy is 0.3-0.5% in different population throughout the world, where the prevalence of epilepsy is in the range of 4-10/1000.[2] Incidence and prevalence are higher in 3rd world countries than the developed world, with higher rates found in the rural as opposed to the urban communities with slightly higher prevalence in male than women with 2/3rd being partial epilepsy and approximately 1/3rd generalised.

According to the World Health Organization (WHO), of the 50 million people with epilepsy worldwide, 80% reside in developing countries [5]. Epilepsy was estimated to account for 0.5% of the global burden of disease, accounting for 7,307,975 disability adjusted life years (DALYs) in 2005[5, 6].

Over the past decade the role of neuroimaging in the diagnosis and management of epilepsy has changed considerably. MRI is more sensitive in diagnosing most of the cerebral pathologies associated with chronic epilepsy with exception of calcification which is better seen in CT [7].

Several laboratory studies should routinely be included in the initial diagnostic workup of seizure — complete blood count (CBC), blood chemistries, liver and thyroid function tests, EEG, and, most importantly, an imaging study of the brain, preferably MRI. CT scanning may be the only feasible study in an emergency or for very young children [8].

MRI is much more sensitive than CT for early detection of causative lesion. Mesial temporal sclerosis, low grade neoplasia, vascular lesions particularly cavernomas, developmental abnormalities particularly abnormalities of cortical neural migration are all likely to be missed by CT but can be easily detected on MRI.

Mesial temporal sclerosis, low grade neoplasias, vascular lesions particularly cavernomas and developmental abnormalities are all likely to be missed by CT. MRI is more sensitive than CT for early detection of causative lesions. Almost all patients with new onset seizure should have a brain imaging study to determine whether there is an underlying structural abnormality which is responsible for seizure disorder. The use of newer MRI methods such as fluid attenuated inversion recovery (FLAIR), Magnetic Resonance Spectroscopy (MRS), Diffusion Weighted Images (DWI) has increased the sensitivity for detection of abnormal cortical architecture including hippocampal atrophy as well as abnormalities of cortical migration and infective aetiologies [8].

MRI is indicated in all patients with epilepsy who appear refractory to pharmacological treatment irrespective of previous imaging study. MRI sequences will usually include T1 weighted thin slice scan, often with hippocampal volumetry, T2 weighted coronal fluid attenuated inversion recovery (FLAIR) and gradient echo sequences (GRE). In patient with suspected CNS infection CT will be performed on emergency basis when MRI is not available, it is usually appropriate to obtain a MRI study within few days of initial evaluation. Neoplasia overall contributes 4% of cases of seizure disorder, rest of the cases are non-neoplastic in 1-20 yrs age group [6, 7]. So according to different literature majority of the seizure disorder in 6-18 yr age group is non-neoplastic [8].

Seizure in later childhood and adolescence represents most common epileptic problem in general practice. Patients with age group less than 6 yrs were not included in our study as though anaesthetic facility for CT scan is available, till date no anaesthetic facility for MRI scan is available in our institute.

Objectives

- To identify CNS lesion in patients with seizure whether it matches with seizure semiology.
- To characterize the lesion and help to plan out whether medical or surgical modalities required
- To help in diagnostic challenge in pharmacologically refractory cases of seizure such as epilepsy syndromes, temporal lobe epilepsy
- To determine the varied role of neuroimaging in seizure disorder

MATERIALS & METHODS

Study Area: The Department of Paediatric Medicine and paediatric neurology, IPGMER, the Department of Neuromedicine including the Epilepsy Clinic and Department of Radiology, Bangur Institute of Neurosciences, IPGMER.

Study Population

Inclusion Criteria

Patient attending Neuromedicine and Epilepsy clinic, Bangur Institute of Neurosciences, Paediatric OPD including Paediatric Neurology, IPGMER with the following criteria

- Age 6-18 yrs
- Male or female
- >1 episode of unprovoked seizure, 24 hrs apart or more, seizures was classified according to International League against Epilepsy (ILAE) criteria

Exclusion Criteria

- Patient with seizure disorder, < 6yr or> 18 yrs
- Patient with seizure disorder diagnosed to be due to neoplastic causes from neuroradiological evidences
- Diagnosed to be a case of neoplastic seizure on the basis of Magnetic Resonance Spectroscopy (MRS), (Choline: creatinine ratio> 2 or choline: NAA ratio >1.3

Sample Size

58 cases, male or female of age group 6-18 yrs with clinical presentation of seizure disorder

Study Period

February 2010—September 2011

Sample Design

All such cases attending Department of Paediatrics including paediatric neurology, IPGMER, Department of Neuromedicine including Epilepsy Clinic, Bangur Institute of Neurosciences

Study design

It was a hospital based cross sectional observational study. Age, sex, characterization of seizure including onset time of attack ,provocative factors, first attack, total no of attacks, frequency of attack, status of consciousness, prodrome, aura, cerebellar symptoms, duration, post ictal phenomenon, history of drug intake, control of attack by drugs, family h/o of seizure, birth history were noted.

Radiological Investigations

MRI investigation of brain in various sequences like T1, T2 in axial and coronal section with or without contrast, coronal fluid attenuated inversion recovery (FLAIR), gradient echo(GRE), diffusion weighted images (DWI), Magnetic Resonance Spectroscopy (MRS), CT scan of brain in axial plane before and after contrast administration.

Study Tool

- With the predesigned proforma with 1.1.5 Tesla (superconductive in nature) MRI machine, model Signs LX horizon of Wipro- GE made was used.
- TOSHIBA made ASTEION 4, 4 slice spiral CT scan machine
- Technique of MRI examination [9-11]
- Patient is placed in supine position with head coil (quadrature coil).
- Localiser taken centering as nasion

Sequence of Obtaining

MRI in different sequences like axial T1 weighted, axial T2 weighted, coronal FLAIR, axial GRE, sagittal T1 and T2 taken through anterior and posterior commisure line as a base line from foramen magnum to top. Sagital and coronal sections are taken perpendicular to above said lines. Slice thickness was normally 5mm with 2 mm gap but in pathology 3mm slice thickness with 1mm gap was taken, in case of coronal FLAIR 3mm slice thickness with 1 mm gap taken perpendicular to temporal lobe in sagittal section. [9-11]

Table-1: Proposed MR Scan Protocol [9-11]

Imaging Plane	Sequence	Comments
Axial	T1 weighted	Anatomical evaluation
Axial	T2 weighted	Parenchymal lesion
Axial	Gradient echo	1. Useful in presence of haemorrhage and calcification in brain 2. To identify bone fracture 3. To identify vascular malformation
Axial	Diffusion Weighted Image	Evaluation of stroke
Sagittal	T1 weighted	Anatomical changes including sellar and suprasellar region
Sagittal	T2 weighted	Parenchymal lesion including sellar and suprasellar area
	Magnetic Resonance Spectroscopy	• To differentiate between non-neoplastic and neoplastic aetiologies • To evaluate temporal lobe Epilepsy
Coronal	Fluid Attenuated Inversion recovery	Sequence of choice for small cortical lesion and temporal lobe lesion
Coronal	T2 weighted	To identify cortical lesion and temporal lobe lesion

Documentation of Any Lesion

When any lesion was detected it was documented at it's side, size location, associated with mass effects or not, presence of oedema or not, associated with gliotic changes or not, associated bony defect or not and the status of the ventricle.

RESULTS

Table-2: Age group and sex distribution among study participants (n=58)

Age Group (Yrs)	Male	Percentage	Female	Percentage	Total
6-9	9	15.52%	11	18.96%	20 (34.5%)
10-12	12	20.69%	1	1.72%	13 (22.4%)
13-15	4	6.89%	5	8.62%	9 (15.52%)
16-18	9	15.52%	7	12.07%	16 (27.6%)

In the present study 34.5% of children belong to 6-9 yrs age group followed by 27.6% of 16-18 yrs group [Table 2].

About 34/58 (58.62%) were male participants. So, there is definite male predilection in our study as depicted by the chart [Fig. 1].

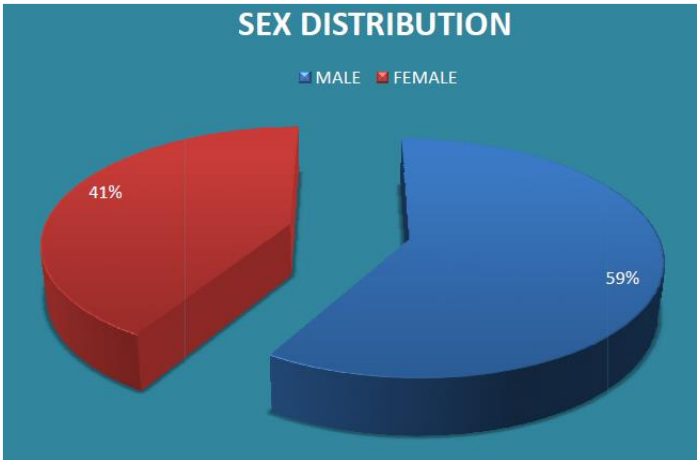

Fig-1: Sex distribution among study participants (n=58)

Table-3: Comparison of CT and MRI in diagnostic usefulness in diagnosing seizure disorders

Total No of Patient	MRI was useful	Percentage of Cases	CT was useful	Percentage of Cases
58	44	75.86%	27	46.55%

Table 2 shows MRI was much more useful compared to CT for detection of lesions in our study as depicted in the diagram [Table 3].

Aetiologies identified through imaging process in the present study were mainly normal (24.14%), mesial temporal sclerosis (Figure 4), congenital structural defect and infective (17.24%) each [Table 4].

Table-4: Different aetiologies of seizure obtained in our study [N=58]

Causes of seizure	No. of patient	Percentage
Mesial temporal sclerosis	10	17.24%
Congenital structural defect	10	17.24%
Infective	10	17.24%
Anoxia	5	8.62%
Normal	14	24.14%
Gliosis	5	8.62%
Miscellaneous causes	4	6.9%

Table-5: Major findings associated with mesial temporal sclerosis (n=10)

Findings	No. of patient	Percentage
Hippocampal atrophy	7	70%
Hippocampal hyperintensity in T2/Flair	6	60%
Dilated ipsilateral temporal horn	7	70%
Indistinct gray white demarcation	4	40%
Atrophy of hippocampal collateral WM	3	30%
Reduced volume of temporal lobe	2	20%

Major findings associated with mesial temporal sclerosis through imaging were mainly hippocampal atrophy (Fig. 5) and dilated ipsilateral temporal horn (70%) followed by hippocampal hyperintensity in T2/Flair (60%), indistinct gray white demarcation (40%), and atrophy of hippocampal collateral WM (30%). Only very few cases reduced volume of temporal lobe (20%) was also observed [Table 5].

Table-6: Comparison of coronal flair with coronal regarding detection of hippocampal hyperintensity as a imaging finding of hippocampal sclerosis (n=10)

	Coronal Flair		Coronal T2	
Hippocampal Sclerosis	No. of patient	%	No. of patient	%
10	10	100%	7	70%

So, coronal FLAIR was much more useful compared to coronaL T2 in our study as depicted in the table 6.

Most common type of seizure was generalised tonic clonic seizures (29.31%) followed by complex partial (25.86%), simple partial (17.24%) and unclassified/ epilepsy syndromes (13.79%) [Table 7].

MRI was better than CT in diagnosing different aetiologies like infective, mesial temporal sclerosis (Fig.4) and congenital structural defect [Table 8/Fig. 2].

Table-7: Seizure Pattern among study cases

Types of seizure	Total no. of patients	Percentage
Complex partial	15	25.86
Simple partial	10	17.24
Generalised tonic clonic	17	29.31
Absence	3	5.17
Myoclonic	2	3.45
Partial seizure with secondary generalization	3	5.17
Unclassified/ epilepsy syndromes	8	13.79

The presenting seizure was classified into different groups as listed below (n=58)

Table-8: Comparison of CT and MRI in diagnosing different aetiologies (n=44)

Causes	No. of patient diagnosed by MRI	No. of patient diagnosed by CT
Infective	10	6
Mesial temporal sclerosis	10	2
Congenital structural defect	10	9
Gliosis	5	4
Anoxia/ hypoxia	5	4
Miscellaneous	5	2

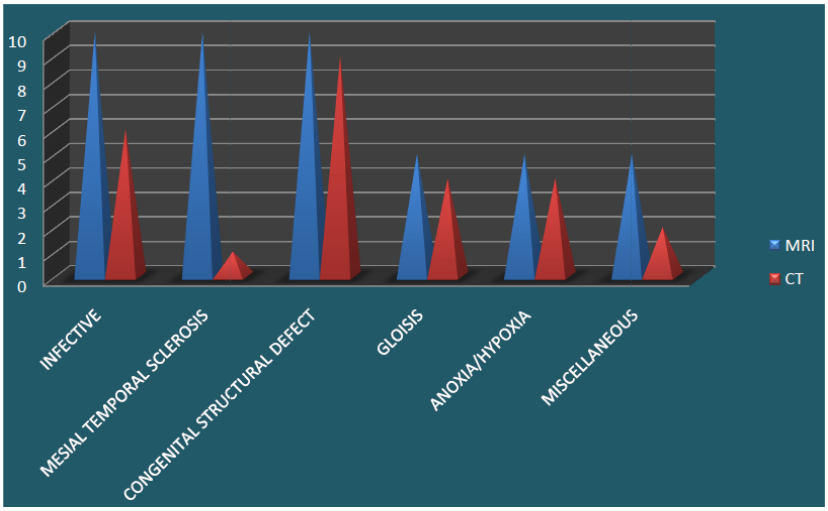

Fig-2: Comparison of CT and MRI in diagnosing different aetiologies (n=44)

Table-9: Congenital aetiologies of seizure (n=10)

Causes	No. of cases	Percentage
Dyke Davidoff Mason syn.	2	22.22
Sturge weber syndrome	1	11.11
Chiari-I malformation	1	11.11
Septo-optic dysplasia	1	11.11
Corpus callosum agenesis	1	11.11
Pachygyria	1	11.11
Arachnoid cyst	2	22.22
Porencephalic cyst	1	11.11

Causes of congenital aetiologies of seizure identified through MRI imaging was mainly Dyke Davidoff Mason syn and Arachnoid cyst (22.22% each) followed by Sturge weber syndrome, Chiari-I malformation, septo-optic dysplasia (Fig. 6), corpus callosum agenesis, pachygyria and porencephalic cyst (11.11% each) [Table 9/ Fig. 3, 6, 7].

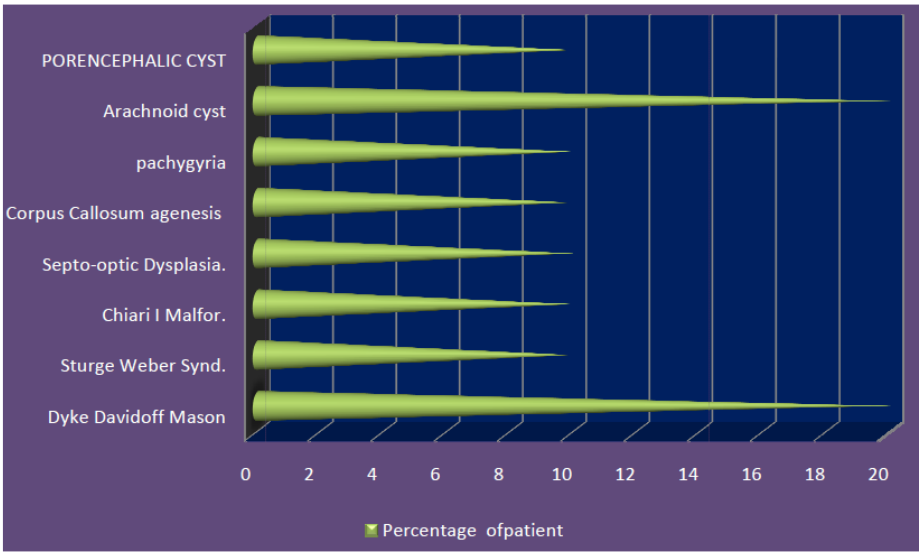

Fig-3: Congenital aetiologies of seizure (n=10)

Table-10: Miscellaneous aetiologies of seizure disorder (n=4)

Causes	No. of the patient	Percentage
Hypertrophic pachymeningitis	1	25%
Subdural hygroma	1	25%
Germinal matrix haemorrhage	1	25%
Rasmussen encephalitis	1	25%

Miscellaneous aetiologies of seizure disorder (n=4) identified through MRI imaging was hypertrophic pachymeningitis, subdural hygroma, germinal matrix haemorrhage and rasmussen encephalitis (25% each) [Table 10].

So, majority of cases with infective aetiology presented with ring enhancing lesion in our study [Table 11/ Fig. 8, 9].

Table-11: Percentage of infective cases presenting as ring enhancing lesion (n= 10)

Total no of cases due to infective aetiology	No. of cases presenting as ring enhancing lesion	Percentage of cases presenting as ring enhancing lesion
10	07	70

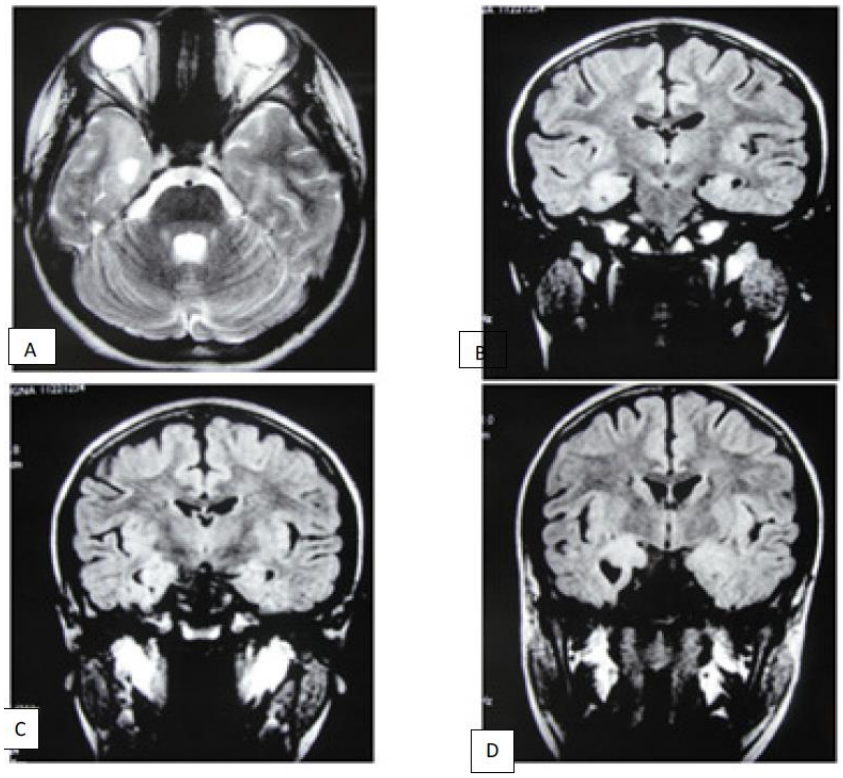

Fig-4: MRI different sequences A -Axial T2 weighted image, B-D coronal flair images showing right sided mesial temporal sclerosis

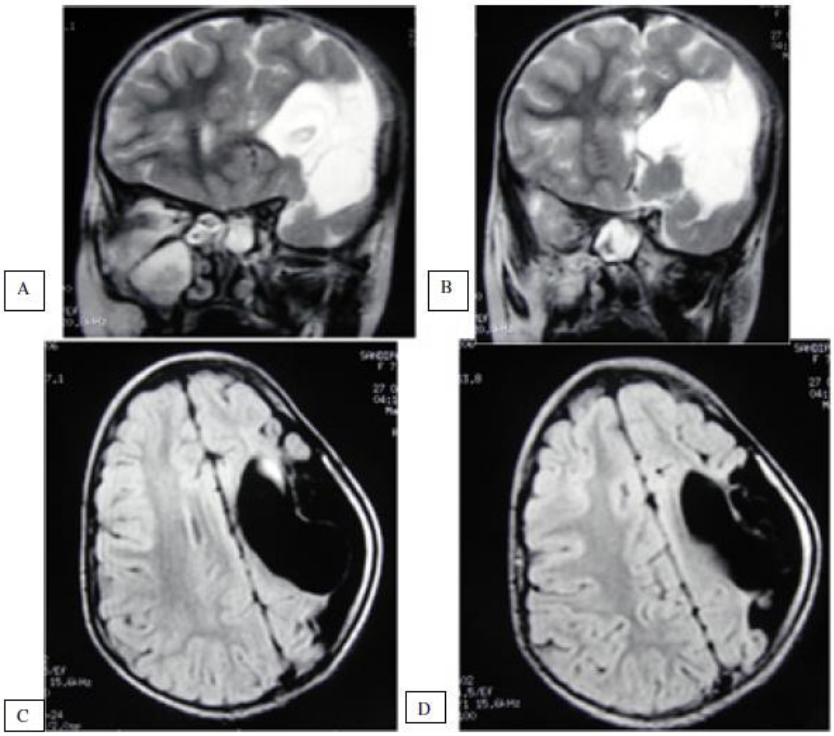

Fig-5: MRI different sequences A, B – Coronal T2 weighted sequences, C,D- Axial FLAIR sequences showing left sided hemiatrophy, encephalomalacia and porencephalic dilatation of lateral ventricle

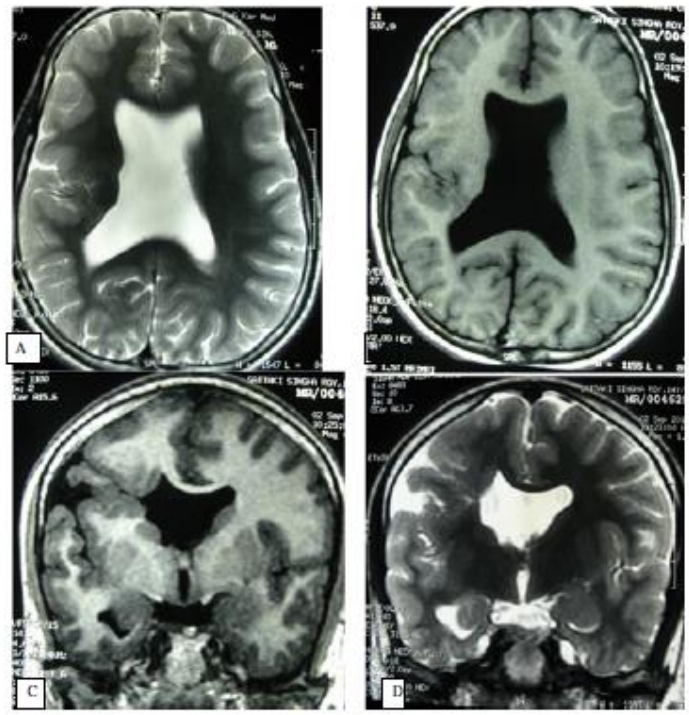

Fig-6: MRI different sequences a-axial T2 weighted, B- axial T1 weighted flair, C-coronal T1 weighted flair and D- coronal T2 weighted images, showing septo-optic dysplasia, type I schizencephaly of right side and heterotopia

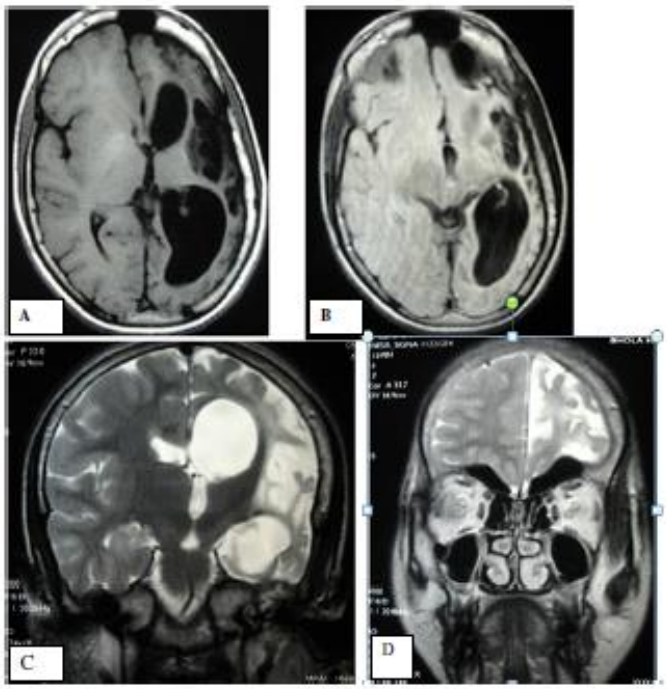

Fig-7: MRI different sequences A- Axial T1 weighted, B-Axial FLAIR, C-D Sagital T2 weighted Images showing Dyke- Davidoff- Masson syndrome

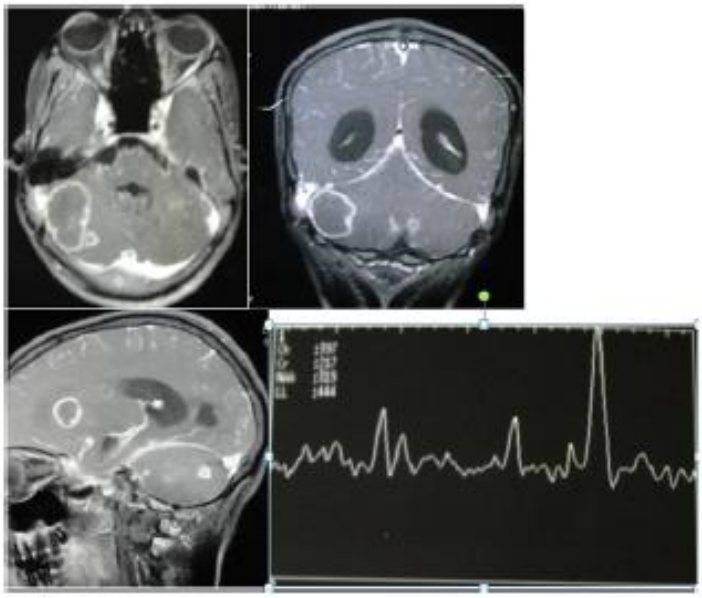

Fig-8: Post contrast MR images in different projection, with MRS correlation showing tuberculoma

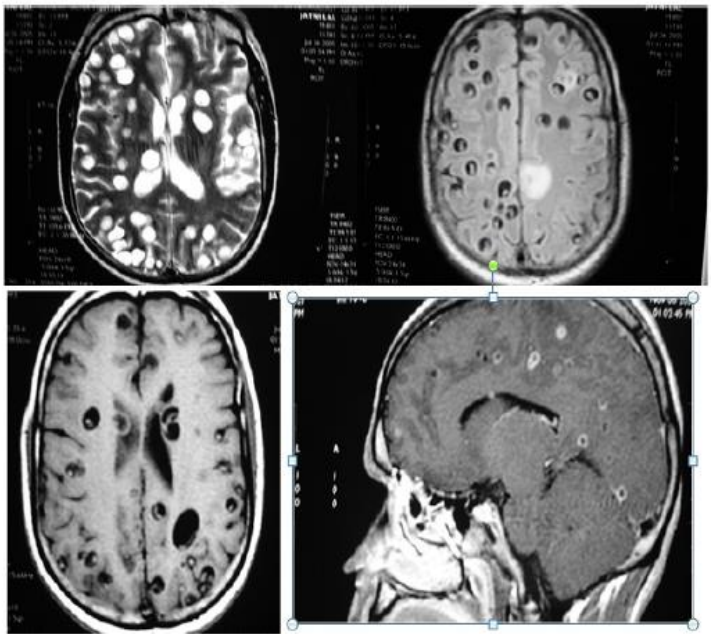

Fig-9: NCC in different MRI projection and sequences

DISCUSSSION

Seizure are common in the paediatric age group and occur in =10% of children. Epilepsy is a condition in which seizure are triggered within the brain. For epidemiology classification purpose epilepsy is considered to be present when two or more unprovoked seizure occurs at an interval greater than 24 hour apart. The cumulative lifetime incidence of epilepsy is 3%, and more than half of the cases begin in the childhood and early adulthood. The annual prevalence of epilepsy is lower 0.5-0.8% because many children outgrow epilepsy. Although outlook for most children with symptomatic seizure is generally good, seizure may signal a potentially serious underlying systemic or central nervous system disorder that requires thorough investigation and management. For children with epilepsy prognosis is generally good, but 20% of patients have persistent seizure refractory to drug and those causes pose a diagnostic and management challenge [1].

In our study most of the cases of symptomatic seizure occurred in 6-12 yr age group comprising of almost 56.9% of all patient. There is also male predilection in our study. Male patient comprises of 58.62% and female patient comprises of 41.38% of patients.

A cross sectional study by Baheti R *et al*. based on CT and EEG finding in patients with generalised or partial seizures done in Western Rajasthan in which 52 children of 1-15 yrs age group with seizure disorder were included; 26 of them were having partial seizures, while the rest were having generalised seizures. Those patients who were having known aetiological factors were excluded from the study. All the patients were subjected to a detailed clinical history and physical examination revealed that 57.7% patient had seizure in 1-10 yr age group and there was definite male dominance among seizure patients [12].

Partial seizure (n = 26), generalized seizure (n=26) male for generalized seizure 18 comprises of (69.2%), and for partial seizure 19 (73.0%) of patients, where female comprises 08 patient for generalized seizure (30.8%) and 07 patient (27.0%) for partial seizure. On the contrary according to Behavioural aspects of epilepsy: Principles and practice by Steven C. Schachter, Gregory L. Holmes, Dorothée Kasteleijn-Nolst Trenité there has been bias to the female sex in several case series [13], but this has not been confirmed on controlled study. But most of these studies were based on Western patient**.** So it can be concluded that there is difference in sex distribution in Western and Indian patients.

Comparison of computed tomography (CT) with Magnetic Resonance Imaging (MRI) for intractable epilepsy was done. In a study of 117 patients with intractable epilepsy who had surgically proven abnormalities, MR had a sensitivity of 86% compared with 28% by CT [14, 15].

In cases of refractory seizures, MRI has significantly greater sensitivity for lesion detection than does CT. In one surgical study, MRI detected the epileptogenic abnormality in 86% versus 32% by CT, and no lesion was detected by CT that was not visualized with MRI. In our study MRI was 75.86% sensitive compared with 46.55% by CT for identification of lesions and no case was diagnosed on the basis of CT which was not visualized on MRI in our study. CT was very poor for particularly detection of mesial temporal sclerosis among 10 patient of mesial temporal sclerosis detected on the basis of MRI, CT was able to detect only 2 cases. In our study CT was as useful as MRI in detection of congenital structural defect.

But according to Bronen RA *et al*. CT was 15% sensitive compared to MRI which was 70% sensitive for detection of congenital lesions [15]. In our study no obvious organic lesion was found in 24.14% of patient. Functional tests such as PET and SPECT, can be co-registered with conventional MRI for better anatomic localization. A localized reduction in cerebral blood flow by SPECT or a decrease in cerebral metabolism by PET has a relatively high sensitivity and moderate specificity for localization of an epileptogenic focus, particularly when involving the temporal lobe. SPECT is unique because it can be performed during ictus (a clinical seizure). PET has better spatial resolution and can use various tracer elements to measure functional disorders. According to Spencer SS *et al*., Ictal SPECT is the single most sensitive method of lateralization in both temporal lobe (90%) as well as extra-temporal (81%) epilepsy [16] A study by Won HJ *et al*. seizure lateralization by MRI based on identification of focal abnormality has been reported to be 55% to 77%, lower than both PET and ictal SPECT. These imaging modalities identify different structural and functional properties of the epileptogenic zone that often provide different and complimentary information [17].

Co-registration of MRI with other functional imaging modalities, including PET and SPECT, has also proven valuable in localization of structural and functional alteration. Ictal SPECT, especially when quantitatively compared to interictal SPECT, has also become a valuable method for accurate localization of the epileptogenic focus. By early intra-ictal intravenous injection of a perfusion dependent radiotracer, it is possible to detect local increases in cerebral blood flow caused by neuronal hyperactivity during the actual seizure. Focal blood flow increase reflects seizure activity, either from cerebral cortex at the seizure onset zone or from seizure spread to other areas. The accuracy of subtraction ictal SPECT co-registered to MRI (SISCOM) in the localization of the seizure focus has been assessed by several studies, comparing it with either invasive ictal EEG, site of surgery, or combined modalities. SISCOM findings can also result in re evaluation of MRI in cases in which the MRI is initially considered normal .MRI, when reinterpreted in light of SISCOM data, may detect subtle abnormalities in non lesional epilepsy. So it can be concluded that addition of ictal SPECT and PET imaging to epilepsy imaging protocol will increase the diagnostic efficiency of imaging modalities [18-20].

In a study performed by Berkovic and colleagues in 1995, sensitivity of MRI for mesial temporal sclerosis was as high as 97%, and specificity was 83%. (Other studies have determined values of 80-90% sensitivity [21]. In our study a significant percent of cases were diagnosed as mesial temporal sclerosis. The imaging findings most frequently observed in our study were

- hippocampal atrophy(70%)
- hippocampal hyperintensity in T2/flair (60%)
- dialated temporal horn (70%)
- Indistinct gray white demarcation (40%)
- Atrophy of hippocampal colateral white matter (30%)
- reduced volume of temporal lobe (20%)

A study by LC Meniers *et al*. regarding temporal lobe epilepsy; MRI appearance in histologically proven mesial temporal lobe sclerosis has shown six MRI features of mesial temporal lobe sclerosis high signal intensity in the hippocampus, reduced hippocampal size, ipsilateral atrophy of the hippocampal collateral white matter, enlarged temporal horn, reduced gray-white matter demarcation in temporal lobe and reduced temporal lobe volume. Heinz *et al*. describe three findings a. decrease in the size of hippocampus as compared to other side b. hyperintensityseen on proton density and on T2 weighted images c. loss of sharp margin between the cortex of the parahippocampal complex and the subjacent collateral white matter, increase signal intensity in the white matter on T2 and volume of white matter [23].

A study by Fatma Mujgan & Ayanci *et al.* regarding clinical, electrophysiological and neuropsychological finding of twenty two children with mesial temporal lobe sclerosis had shown important findings like hippocampal atrophy, increased signal intensity in T2 weighted MR images and dilatation of ipsilateral temporal horn as gold standard diagnostic criteria for detection of mesial temporal sclerosis.

CONCLUSION

After studying 58 numbers of patients we have come to the following conclusions.

Non-neoplastic aetiologies of seizure disorder in 6-18 yrs age group are of various groups among them congenital structural defects, infective aetiologies and mesial temporal sclerosis is the major contributor. There is definite male preponderance in this age group in our. Country and 6-9 year age group is the most common age group of seizure presentation in our study. MRI is a very effective tool in detecting the structural lesions responsible for seizure disorder. Coronal FLAIR sequences were more informative compared to coronal T2 for identification of mesial temporal sclerosis and must be included in epilepsy imaging protocol.

MRI is superior investigation modality compared to CT for detection of structural abnormalities associated with seizure disorder. Hippocampal atrophy and dilated ipsilateral temporal horn are the most frequently observed findings in temporal lobe sclerosis. Ring enhancing lesions are the most frequent imaging presentation for infective aetiologies of seizure. There will be future scope of functional MRI, ictal SPECT, PET imaging and fusion with CT and MRI in MRI negative cases.

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