

Role Of Magnetic Resonance Imaging In Mesial Temporal Lobe Epilepsy With Special Reference To Hippocampal Volumetry And T2 Relaxometry

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Abbreviations:

- AED's : Antiepileptic Drugs
- AMPA : Alpha Amino-3-Hydroxy-5-Methylisoxazole-4-Propionic
- Acid Receptor.
- EEG : Electroencephalography
- EZ : Epileptic Zone
- HS : Hippocampal Sclerosis
- HV : Hippocampal Volume
- HVD : Hippocampus Volume Difference
- HVR : Hippocampus Volume Ratio
- ILAE : International League Against Epilepsy
- LTLE : Lateral Temporal Lobe Epilepsy
- MEG : Magnetic Encephalography
- MTLE : Mesial Temporal Lobe Epilepsy
- NMDA : N-Methyl-D- Aspartate Receptor
- NTLE : Neocortical Temporal Lobe Epilepsy
- TE : Echo Time
- TI : Inversion Time
- TLE : Temporal Lobe Epilepsy
- TR : Repetition Time
- WHO : World Health Organization

1. Introduction

Epilepsy is a familiar neurological disease. Antiepileptic drugs generally manage most of epilepsy although in 30% of cases they are not of benefit. Epilepsy word was derived from the word Epilepsia which means "to take hold of or to seize" in Greek literature. In ancient cultures of China, Egypt, and India, epileptic seizures were mentioned before [1]. The first book on epilepsy was written almost 2500 years ago by Hippocrates. In that book, the previous ideas regarding epilepsy etiology were changed and mentioned excessive phlegm that caused abnormal brain consistency as the cause of epilepsy. Epilepsy is a group of syndromes with different clinical features, not a single disease that was

considered before. But in all cases associated with abnormal electrical findings in the brain. There is pathological electrical activity in neurons of the brain which gives rise to seizure [2]. The main pathophysiology of seizure is relative state of hyperexcitability due to loss of normal regulation of neuronal excitation and inhibition. Multiple episodes of seizures which are not increased by an acute systemic or neurologic insult for chronic period is considered as epilepsy, however it does not have any specific pathology on its own. In the adult population, Mesial temporal lobe epilepsy (MTLE) is the most common type of epilepsy [3,4]. Surgery is usually very effective in cases of MTLE, as they are generally refractory to medical treatment. However, no sufficient data are known for failure [5]. In the causes of partial epilepsy, TLE is the most common [6]. On the basis of imaging and histopathological findings there are two types of MTLE: First is TLE with mesial temporal lobe sclerosis (TLE-MTS, about 60–70%), where atrophy and altered MR signals can be seen on imaging and severe neuronal loss in the histological examination, and second is TLE with normal-appearing hippocampus on the MRI (TLE-no, about 30–40%) and on histological examination characterized by no or minimal neuronal loss [2,7]. The most common pathology of MTLE that is hippocampus sclerosis can be identified on MRI, especially sensitivity increases on including quantitative parameters also for hippocampus evaluation. Bilateral hippocampal sclerosis and mild hippocampal sclerosis which are not detected on visual conventional MRI can be detected using quantitative methods of hippocampus volumetry. Similarly, T2 relaxometry can also increase detection rate of HS on MRI. Histopathologic findings of HS has good correlation with quantitative methods like hippocampal volumetry and T2 Relaxometry [4]. Newer techniques nowadays included in epilepsy protocols like MRI diffusion and MRI perfusions. Another technique like Functional MRI has also included for eloquent cortex mapping and language lateralization in

presurgical investigation. Surgery is becoming treatment modality throughout the world for MTLE cases which are refractory to anti-epileptics. Focal and refractory epilepsy is most commonly caused by MTLE [8]. Among these patients 60% have chance of been seizure-free after surgery, therefore identification of the cause on MRI is necessary. Precise localization of seizure focus is critical because of the advent of viable surgical approaches to the management of epilepsy and potential for future less invasive treatment modalities such as gamma knife radiosurgery. In most of the studies on 1.5 T, MR has shown higher sensitivities of quantitative methods like hippocampal volumetry and T2 Relaxometry in comparison to qualitative methods. Due to new advancements in MRI these days 3T MR is used in many epilepsy higher centers increasing the sensitivity for detection of HS. However there is no significant difference in the hippocampal volume measures of 1.5 and 3T but the quantitative measures in 3T MRI are able to detect ultrastructural details of HS pathology which are not detected on 1.5 T increasing its sensitivity. The main aim of our study is to evaluate the role of hippocampal volumetry and T2 Relaxometry in mesial temporal lobe epilepsy, and compare the relative value of visual assessment, hippocampal volumetry, and T2 relaxometry individually and in combinations, in the diagnosis of Hippocampal sclerosis [4]. On the other hand, we also aim to provide normative MR hippocampal volumetric data for the northeast Indian population.

1.1. Aims and Objectives

The presents study **"ROLE OF MAGNETIC RESONANCE IMAGING IN MESIAL TEMPORAL LOBE EPILEPSY WITH SPECIAL REFERENCE TO HIPPOCAMPAL VOLUMETRY AND T2 RELAXOMETRY"** was carried out in the Department of Radiodiagnosis, Assam Medical College & Hospital,

Dibrugarh, with the following aims and objectives:

- To evaluate the role of hippocampal volumetry in mesial temporal lobe epilepsy.
- To evaluate the role of T2 relaxometry in mesial temporal lobe epilepsy.
- Correlating these MRI findings with EEG.

1.2. Anatomy and Physiology

1.2.1. Temporal Lobe and Limbic System

Among the four lobes of brain temporal lobe is one of them. It is present in the middle cranial fossa. The anterior and inferior boundaries of the temporal lobe are formed by temporal lobe. Sylvian fissure separates the upper surface of the temporal lobe from the frontal and parietal lobes. In the posterior part, it is separated from occipital and parietal lobes by an imaginary lateral parietotemporal line which runs down from the posterior edge of the Sylvian fissure (Figure-1) [9]. A line that connects the inferior fork of the Sylvian fissure to the superior-lateral aspect of the choroidal fissure temporal horn complex forms its medial boundary [10]. The superior and inferior temporal sulci which are present on lateral surface of the temporal lobe divides the lateral surface into superior, middle, and inferior temporal gyri. There is lateral occipitotemporal gyrus which is the extension of these curves onto the inferior surface of the brain and extending posteriorly into the occipital lobe. Superior temporal gyrus forms the superior surface of the temporal lobe, which forms the floor of the lateral sulcus. A cortical area, planum temporale is present posterior to the primary auditory cortex. Planum temporal is generally larger on left than on the right side in men, but not the same in women [11]. The parietal lobe and occipital lobe are in continuity with the posterosuperior and posterior part of temporal lobe respectively.

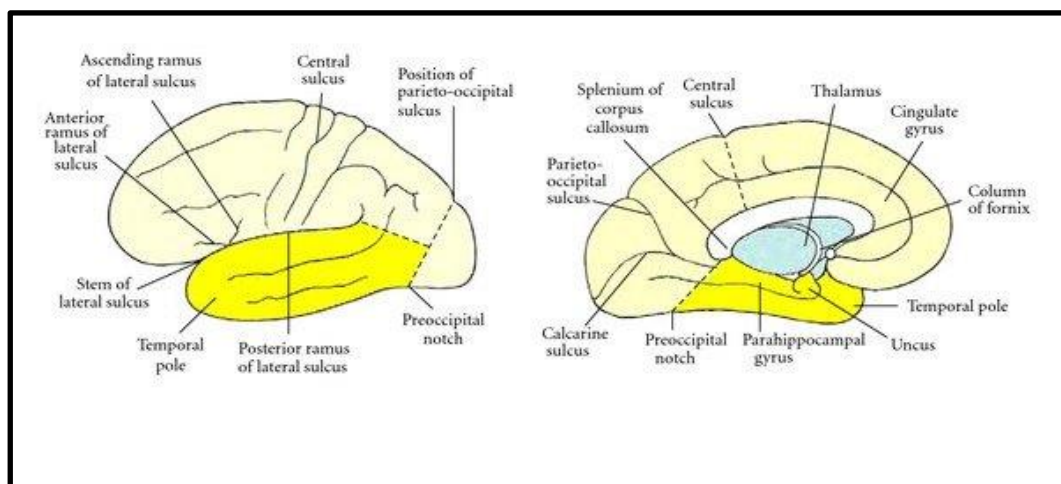


Figure 1: Broadly Temporal Lobe is Divided into Two Lobes:

- **Neocortex** (also known as temporal lobe) Standard cerebral cortex which includes lateral and inferolateral surfaces.
- **Mesial temporal lobe** (also known as limbic lobe) includes:

The hippocampus, Amygdala, Parahippocampal gyrus, Dentate gyrus and

Uncus.

Three sets of C-shaped structures that contain grey and white matter both form the limbic system [12]. Portions of all the lobes of cerebral hemispheres were included in it and it is present deep within the brain parenchyma [13,14]. The limbic system (Figure 2) can be easily studied as three concentric arches of grey and white matters as follows:

(A) The Outer Arc: (also called the limbic gyrus) It includes:

- subcallosal area,
- cingulate gyrus,
- isthmus of the cingulate gyrus, and
- parahippocampal gyrus, which includes uncus and subiculum.

The subcallosal area includes a cluster of small septal nuclei that lie immediately anterior to the para terminal gyrus and anterior commissure.

(B) The Middle Arc or Broca's Intralimbic Gyrus which includes – Hippocampus, Paraterminal Gyrus, and Indusium Griseum.

- The wedged area between septal nuclei and anterior commissure forms para terminal gyrus.
- Gray and white matter tracts named medial and lateral longitudinal stria extending from para terminal gyrus from the indusium griseum. The superior surface of the corpus callosum is closely applied to indusium griseum. It continues with tail of hippocampus inferiorly and presents around splenium of corpus callosum posteriorly.
- Hippocampus – discussed in detail below.

(C) The Inner Arc: Formed by:

- The mammillary bodies
- Fornix
- alveus and
- fimbria

1.3. Embryology

According to Humphrey, before the 10th week of development, the dentate gyrus and cornu ammonis are thin rudimentary structures positioned successively along the posterolateral aspect of the diencephalon (the posteromedial wall of the lateral ventricle). At the 10-week stage, a broad shallow hippocampal sulcus is present along the posterolateral aspect of the diencephalon. This shallow hippocampal sulcus appears when the telencephalic wall of the primordial dentate gyrus becomes thicker than that of the cornu ammonis. The sulcus is deeper and it shifts toward the junction of the cornu ammonis and dentate gyrus at 10 to 11 weeks as the dentate gyrus increases in thickness. At 12 to 14 weeks, the increasing thickness of the dentate gyrus causes it to rotate toward the cornu ammonis, and the hippocampal sulcus becomes progressively deeper and more sharply defined. As the sulcus deepens it becomes oriented more toward the junction of the cornu ammonis with the subicular region. When the dentate gyrus and cornu ammonis approach each other, a diffuse zone of scattered

cells appears deep to the sulcus. In the human fetus, this diffuse zone is a well-defined triangular area by 13 to 14 weeks and it lies between the definitive molecular stratum of the dentate gyrus and the molecular stratum of the cornu ammonis. There is bulging of the medial wall of hemisphere into lateral ventricle due to the growth of the dentate gyrus and cornu ammonis. The hippocampal sulcus is best developed by 15 to 16 weeks, hippocampal sulcus relation to the surrounding structures is similar to that of the adult brain by 18 to 21 weeks [15].

1.4. Hippocampus

(Figure-3) Part of the limbic system present in temporal lobe which is functionally involved in-memory processing, learning, and emotions [9]. The gyrus dentatus and the cornu ammonis are the two allocortex laminae which create a bulge in temporal horn of lateral ventricle because they are rolled up inside each other. Hippocampal sulcus separates these parts [16]. The subiculum is present below the sulcus. A zone is present which separates neocortex from hippocampus which is a part of the allocortex (archicortex). It has three divisions into hippocampus proper (Cornu ammonis; CA), dentate gyrus (DG), subiculum, and entorhinal area (EC) on the basis of anatomy. On general appearance it resembles a sea-horn [17]. Along whole length of the parahippocampal gyrus, entorhinal area is present which is cortex adjacent to the hippocampus [18]. The transitional zone is present between the entorhinal and hippocampal cortices known as subiculum. The consolidation of memory is the best-understood function of the hippocampus till now. The club-shaped structure of hippocampus is divided into three-part – **head, body, and tail** in sagittal plane.

• Head of Hippocampus

It is directed anteriorly- inferiorly- then medially and forms the largest part of the hippocampus. Its shape resembles a feline paw- "pes hippocampi" due to the presence of three or four interdigitations.

The intraventricular region which includes digitations and extra-ventricular region which includes uncus is the division of head of the hippocampus.

• Body of Hippocampus

It is located at the atrium and forms the middle part of hippocampus.

• The tail of the Hippocampus

It is present at the medial part of floor of atrium and is slender. It fuses with calcar avis in medial part.

The cornu ammonis (or hippocampus proper) and the dentate gyrus are two gray matter folds which interlock in each other and form hippocampus [19].

• Dentate Gyrus

It is like a pointed wedge or semicircular structure around end of hippocampus proper and is a layer of small granule cells.

• Cornu Ammonis

It is divided into four portions- CA1 also known as Sommer's sector, very small zone CA2, CA3, and zone which lies below dentate gyrus called CA4. "Hippocampus proper" is used to include all the four CA fields, and term "hippocampal

formation" is used to include hippocampus proper dentate gyrus and subiculum.

- **The Amygdala**

Is present between uncus and parahippocampal gyrus in medial temporal lobe and is of the shape of almond.

- **The Mammillary Body**

It is the part of the limbic present on undersurface of brain as pair of small round bodies. The medial mammillary nuclei and the lateral mammillary nuclei are the two nuclei. Processing of recognition memory is the function of mamillary bodies along with the anterior and dorsomedial nuclei in the thalamus.

- **Fornix**

It is present from the hippocampus to mammillary body in a form of fibrous band of nerve fibers of arch shape.

1.5. Blood Supply of Hippocampus

The anterior, middle and posterior hippocampal arteries are the three main arteries supplying the hippocampus which are the branches of a posterior cerebral artery. The hippocampal head is supplied by anterior hippocampal artery and body & tail of hippocampus are supplied by the middle and posterior hippocampal arteries [19]. Superficial hippocampal veins drain the intrahippocampal veins which provide venous vascularization to hippocampus [16].

1.6. Physiology

1.6.1. Mesial Temporal Lobe (Limbic System)

Olfaction was considered the first initial function of the hippocampus as the hippocampus receives direct inputs from the olfactory bulb. But later on this idea was proven to be false [17].

1.6.2. The Function of Hippocampus

In the adult life hippocampus is one of the regions of brain where neurogenesis continues. Inhibition, memory, and space are the three main functions of hippocampus known over years in literature.

But now due to recent researches, it is known that hippocampus is also involved in:

- Spatial navigation
- Emotional behavior
- Regulation of hypothalamic functions

1.7. Learning and Memory

Learning, memory, and spatial navigation are important functions of hippocampus [20-22]. Awareness about conscious knowledge is due to the connections between the hippocampus and neocortex. Polysynaptic and direct pathways are the two major pathways for learning and memory loop. Hippocampus gets afferent fibers from parietal, temporal, and occipital areas via entorhinal cortex and then to dentate gyrus→CA3→ CA1→ subiculum→ alveus→ fimbria→ fornix→ mamillothalamic tract→ anterior thalamus→ posterior cingulate→ retrosplenial cortex in polysynaptic pathway. However, it gets its input from the temporal association cortex through perirhinal and entorhinal area to CA1 in the direct intra-hippocampal

pathway. Episodic and spatial memory is related to direct intra-hippocampal pathway while semantic memory is related to the polysynaptic pathway [23].

1.7.1. Other Roles

- Motor behavior can be affected due to the ventral striatal loop in which hippocampus is a part [24]. As hippocampus and amygdala both have reciprocal connections, therefore can influence each other and so can affect emotional behavior which is regulated mainly by amygdala. Adrenocorticotrophic hormone release can be affected by hippocampus because of projections to hypothalamus. On damage to the hippocampus of one hemisphere there can be retention of memory because of bilateral symmetry as the brain has a hippocampus in both cerebral hemispheres [11,23]. However, anterograde and retrograde amnesia is common on severe damage to both the hippocampus [23].

1.8. Pathology

- **Aging**

Extreme effect on many types of cognition is seen in age-related conditions such as Alzheimer's disease (in which the earliest sign is hippocampal disruption) [25]. Hippocampal dysfunction is considered to be the cause of age-related declines in memory. Limiting effect on medial-temporal lobe cytoarchitecture is now consider the more accurate cause according to recent studies [26].

- **Alzheimer's Disease**

Many types of cognition are affected in it and hippocampal deterioration is the main cause associated [25].

- **Stress**

Knowledge about stress and brain structural and functional plasticity revealed the role of the hippocampus and other interconnected brain regions like amygdala and prefrontal cortex. Both genomic and rapid non-genomic actions of circulating steroid hormones in the brain were known by the discovery of dendritic and spine synapse remodeling and neurogenesis in the dentate gyrus. Epigenetic effects of early-life experiences can be understood by the hippocampus which serves as a gateway [27].

- **Schizophrenia**

Cerebral cortex pathological changes can be seen in patients suffering from schizophrenia. Synaptic organization and connectivity abnormalities along with hippocampal changes like reduction in the hippocampal size have also been described [28]. Changes in long term memory are commonly seen in people with schizophrenia. However, no significant data is present regarding role of hippocampal changes in causing the psychotic symptoms [29].

1.9. Temporal Lobe Epilepsy (TLE)

The medial or lateral temporal lobe is the site of origin of seizures, in which focal seizures is most common type. Because of strong interconnections the seizure often extends and involves both areas including neighboring areas on the same side of the brain as well as contralateral homologous brain areas. Mesial temporal lobe epilepsy (MTLE) which arise in the hippocampus, parahippocampal gyrus and amygdala and lateral temporal lobe epilepsy (LTLE) which arise in the

lateral neocortex are two main types of the TLE. Hippocampal sclerosis (scarring) is the most common pathology associated with mesial TLE which shows neuronal cell loss and reactive gliosis in the hippocampal area on histology. Neurogenesis occurs throughout life in hippocampus and it is most electrically excitable part of brain parenchyma [30]. TLE may be a progressive condition where seizures become more resistant to medications over time. There is suspected complex pathology of hippocampal sclerosis including genetic, developmental and environmental components which are not known in proper detail in literature. Hopefully, prospective neuroimaging studies which can be used to follow its evolution. Malformation of cortical development, low-grade gliomas, and vascular/ traumatic lesions are the other causes of TLE. TLE can also be affected by strokes, cortical malformations, multiple sclerosis plaques, etc. and be the cause of seizures from this area. So the temporal lobe epilepsies could be caused by many etiologic factors. Rolandic epilepsy is the most common focal epilepsy syndrome in the pediatric age group. This "benign childhood epilepsy with centrotemporal spikes" has an excellent prognosis regarding the seizures, which usually resolve at puberty, and EEG, which will be normalized.

1.10. Function of Amygdala

• Fear

The amygdala is also involved with mood and the conscious emotional response to an event, whether positive or negative.

1.11. Review of Literature

1.11.1 Historical Prospective

Epilepsy word was derived from the Greek, meaning to "seize upon" or "taking hold of". Epilepsy had a documented history before the birth of Lord Jesus and was known to Romans and Greeks. First neurosurgery procedure, craniotomy was said to be done on the contralateral side to site of seizures occurrence in brain for treatment of this phlegm which causes the disease; this was described in the book on sacred disease by Hippocrates. In Assam and India, it is known as "mirgee". Initially, epilepsy was thought to be a divine punishment in terms of religious superstitions, until the newer advances in the field of medicine in around 18th -19th century [31,32]. Epilepsy was divided into two terms idiopathic and sympathetic epilepsy with sensitive aura by Maisonneuve. Petit and grand mal epilepsy were the other classifications of epilepsy on the basis of clinical and postmortem studies done by Esquirol with Bouchet and Cazauvieilh [32]. But in the field of epilepsy work of John Hughling Jackson, was of main epileptology scientific base [32]. On the basis of pathology and anatomy he studied epilepsy and his studies formed the newer version of epilepsy which we consider in our modern scenario. He also defined epilepsy as: "Rapid and local discharges of grey matter which are for occasional, sudden and excessive duration," [32].

However, the cortical localization of the epilepsy concept was given by William Gowers, J. Hughlings Jackson, Victor Horsley, and David Ferrier.

1.12. Electroencephalogram Development

Fritsch and Hitzig studied the first correlation of electric stimuli with brain activity by his study on dogs where he was able to produce seizures by electrical stimulation of cortex of animals. On the basis of contact of a single electrode, the technique of EEG was discovered by Berger. Later on, this technique was modified by multiple researchers to localize the seizure focus. Spikes and waves complex pattern was discovered by the study of Prince and his research team [31]. Hippocampal sclerosis which was considered the main cause of temporal lobe epilepsy was first found by Falconer. There was advanced researches in the field of localization of seizures by EEG over these last 30 years [31].

1.13. Epilepsy

In the year 1993 ILAE defined epilepsy as a condition of recurrent (two or more) epileptic seizures which are unprovoked by any immediate identified cause [33]. Epilepsy was present in around 50 million population of the world and in developing countries in around 50% population according to the World Health Organization (WHO). According to the statistical data of 2005, epilepsy accounts 0.5% of the global burden of disease. There was 1% prevalence of epilepsy in Indian population and was comparatively more in rural population [33]. The study by Bharucha et al stated higher prevalence of epilepsy in male in comparison to females. However, the exact numerical data about prevalence of intractable seizures in India is lacking. Another type of reflex epilepsy called Hot water epilepsy (HWE), due to contact of head with hot water was noted in rural part of South India and account for 3.6-3.9%. An exaggerated discharge of nerve cells causes seizure. On the basis of area involved in these discharges seizures can be of two types: focal/partial seizures which affect localized lesion or focus of brain and generalized seizures which involve whole brain or spread from the small area (focus) to the whole brain and spinal cord [33]. Convulsion, fit or attack are the other names of seizures use by the general population. But generally these terms are used for tonic-clonic muscle movements. International League against Epilepsy (ILAE) in 2017 updated a newer classification of seizure as:

• Generalized Seizures

In the general population it is the typical type of epilepsy with generalised tonic-clonic type of convulsions [34]. But a range exists in it from absence seizures to myoclonic seizures and less common types like atonic seizures which cause falls or drop attacks and **epileptic spasms**.

• Focal Seizures

On the basis of the site of origin of the abnormal electrical discharges along with the extent and spreading speed of these discharges in the brain causes different types of symptoms in focal seizures. However, brain imaging can be normal in 1/3rd of cases of focal seizures.

• Focal and Generalized Seizures

Characterized by evidence of both types of seizures as the name suggests and usually detected by abnormal EEG findings.

• **Unknown**

When the type and cause of epilepsy cannot be defined by doctors.

1.14. Epilepsy Syndromes

These are of various types on the basis of different types of clinical features which include the type of seizures, EEG changes, pathological findings on brain imaging and lastly genetic analysis. Different types of presentation of epilepsy syndrome were described by ILAE on two websites of ILAE namely www.epilepsydiagnosis.org and website of the ILAE educational journal *Epileptic Disorders* (www.epilepticdisorders.com). Generalized epilepsies are most common form of epilepsy syndromes which include childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy and generalized tonic-clonic seizures alone. Because exact cause and genetic basis are not known for these, so also referred as “idiopathic generalized epilepsies”. Focal epilepsy syndromes are the other type which have self limited course and present in children. The diagnosis of the condition is necessary for the effective treatment of the condition [35].

1.15. Treatment-Resistant Epilepsy

There are treatment-resistant seizures also known as intractable seizures seen in nearly 20% of population which do not respond to anti-epileptic drugs even after so much advancement in medical field. We call it as drug resistance when there is ‘failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules – whether as monotherapy or in combination – to achieve sustained seizure freedom’. At the time of diagnosis increase number of seizures and symptomatic epilepsy (epilepsy with a known, often structural cause) are the risk factors for development of drug-resistant epilepsy. However the exact cause of drug-resistant epilepsy is not known yet. Reduced uptake of AEDs due to genetic predisposition, reduced expression of AED targets or different mechanisms of epileptogenesis in people are the few probable causes of AED resistant. MRI is required in all these patients to rule out any underlying brain pathology. Hippocampus sclerosis or mesial temporal sclerosis is the most common pathology detected in these cases on MRI which can be treated by surgery. Surgery in these cases is very effective to make the patient's seizure-free. Nowadays, they are also treated by repeated stimulation of the vagus nerve by battery-powered devices called Vagus nerve stimulators which are surgically implanted [36].

1.16. Temporal Lobe Epilepsy

Partial seizures most commonly originate from temporal lobe accounting for around 2/3rd of all intractable seizures. In the 19th century Jackson was the first to characterize seizures originating near uncus and called them as uncinate fits. In 1985 temporal lobe epilepsy was defined by the ILAE as a condition of recurrent unprovoked seizures which originates in the medial or lateral temporal lobe. Seizures originating in amygdalohippocampal area (mesialbasal limbic or rhinencephalic) and lateral temporal area were

also included in the classification of seizures by ILAE and later included in TLE category under heading of neocortical TLE (NTLE). Specific EEG patterns along with emotional, mental, and autonomic phenomena for seizures originating in the temporal lobe were called psychomotor epilepsy by Gibbs and Lennox [37,38]. According to the classification of the epilepsies given by ILAE, temporal lobe epilepsy divided into three etiologies which include cryptogenic (presumed unidentified etiology), idiopathic (genetic), and symptomatic (cause known, eg, tumor). Temporal lobe epilepsy was divided into two groups MTLE and NTLE previously by ILAE but now MTLE included under “distinctive constellations/ electroclinical syndromes” in revised classification of ILAE [39].

1.17. Two Main Types

• **Mesial Temporal Lobe Epilepsy (MTLE)** is the most common epilepsy in adults and can be localized. They originate from older medial (limbic) temporal cortex which includes olfactory areas, amygdala, hippocampus, and Parahippocampal gyrus. Febrile seizures (frequently prolonged ones), meningitis, encephalitis, or head trauma are common risk factors. The most common lesion seen in MTLE is mesial temporal sclerosis/HS and usually presents with intractable/ drug-resistant seizures which can be treated by surgery. Complex partial seizures are the most common type of seizure seen in them [40].

• **Lateral Temporal Lobe Epilepsy (LTLE)** is epilepsy which originates in newer lateral (neocortical) temporal cortex. Clinically they manifest as visual and auditory hallucinations from discharges arising from the lateral temporal lobe. Most commonly it is caused by head trauma, and other causes include low-grade tumors, cortical dysplasia, and infection.

1.18. Epidemiology

There is no significant epidemiological data available on MTLE. One data given by Hauser and Kurland showed an incidence rate of TLE was 10.4 per 100,000 between 1945 to 1964 and 6.5 between 1935 to 1944. Incidence rates of epilepsy were found to be 54.3 and 34.7, respectively for whole population during same time interval. The prevalence of TLE in 1960 was 1.7 per 1,000 people in the same study. In surgical centers most common referred epilepsy was MTLE. Accounting for around 50 to 73% of all cases assessed. The good surgical outcome may be the reason for high incidence of these patients in epilepsy surgical centers. 24% of patients referred to tertiary care centers had TLE was found in study of Semah No sex prevalence was found in TLE, they were usually equally distributed in males and females [37]. Overlapping may be there in MTLE and LTLE sometimes. Around less than 10% of patients of TLE have LTLE, but significant data is not available.

1.19. Pathophysiology

Hippocampal sclerosis was found as the most common cause in various neuropathological studies. On brain imaging of most of the intractable epilepsy patients, HS is commonly seen. There is no data on exact etiology of this type of epilepsy. However, severe childhood illness (infection,

febrile convulsions, status epilepticus, SE) and hippocampal atrophy were found as relatable cause in several studies. History of initial insult is not necessarily present in all cases. Recurrent seizures may sometime cause progressive damage to the hippocampus and were seen as a cause in few newer studies. Even though the accurate cause is unknown but there is a good seizure-free surgical outcome in patients who undergo hippocampal surgery. The cellular damage in the hippocampus, amygdala, and entorhinal cortex are collectively called mesial temporal sclerosis. There is a newer histological classification given for HS: ILAE hippocampal sclerosis type 1- in which there is pyramidal cell loss in lateral (neocortical) temporal cortex [37]. Clinically they manifest as visual and auditory hallucinations from discharges arising from the lateral temporal lobe. Most commonly it is caused by head trauma, and other causes include low-grade tumors, cortical dysplasia, and infection.

• Interictal EEG in MTLE

There can be various forms like nonepileptiform abnormalities, epileptiform discharges, or both.

In non-Epileptiform two forms of activities can be seen:

Focal Dysrhythmia/Slowing. or

Temporal Intermittent Rhythmic Delta Activity (TIRDA). which is most specific to TLE.

While in epileptiform discharges spikes and sharp waves are seen.

• **Ictal Scalp EEG in MTLE:** Nonspecific beginning of low-voltage fast (electro decrement) activity, with focal or regional background attenuation, is seen. In NTLE absence of the ictal scalp discharge is more common than in MTLE [39].

• **Video-EEG Telemetry:** It can be used for the diagnosis of temporal lobe epilepsy in presurgical evaluation but, further research is required in this field.

• **Postictal EEG Changes in MTLE:** Multiple artifacts that are seen in ictal EEG can be removed in post-ictal EEG.

• **Intracranial Recordings in MTE:** It has good temporal resolution and is artifact-free. It increases the sensitivity of diagnosis of MTLE by EEG.

1.20. Structural Imaging

• Role of MRI in Mesial Temporal Lobe Epilepsy

• **Conventional MRI:** atrophic hippocampus along with the hyperintensity on T2/FLAIR sequences are the hallmark features of mesial temporal lobe sclerosis on MRI. These two findings are called primary MR findings of HS. There is 70% to 90% probability of these patients to be seizure-free after temporal lobectomy. While in patients without these primary features, have 50% chance of being seizure-free post-surgery. However, in some patients these findings are absent or equivocal. Then other signs of MTS on MR called secondary MR features are used for diagnosis in conjunction to increase the sensitivity of detection. Secondary MR findings include loss of normal internal architecture of

the hippocampus (which is It helps in the diagnosis and classification of epilepsy. Localisation of site of seizure origin can be seen by EEG like in temporal lobe epilepsy (TLE), sites may be medial or lateral temporal lobe. Gibbs in 1935 were the first to describe rhythmic sharp waves and 6 per second waves.

1.21. EEG Can be of Different Types

• Interictal EEG in MTLE

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1.22. Structural Imaging:

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[44,48,49].

1.23. Other New Techniques

• **MRI Spectroscopy:** single-voxel studies of the hippocampus and temporal lobe are in use but still in the early stages of evaluation. It helps in lateralizing the seizure focus in TLE by demonstrating reduced NAA levels in the ipsilateral hippocampus and mesial temporal lobe.

• **Perfusion MRI:** it is a non-invasive and non-irradiating supplementary method of localization of seizure using arterial spin labeling (ASL)-based magnetic resonance (MR) perfusion. Reversibility or evolution into sclerosis can be seen on interval imaging [50].

• **Diffusion MRI** is a quantitative method, which can express the pathologic changes of the hippocampus when conventional imaging methods fail to lateralize the lesion side. An increase in diffusivity in the HS is seen due to neuronal loss and atrophy which leads to the expansion of the extracellular space with fluid. The microstructure was found to be abnormal in multiple tracts of MTLE patients, including the anterior/posterior corpus callosum, cingulum, external capsule, and uncinate fasciculus in one meta-analysis done on MTLE cases [51,52].

• **Functional MRI:** fMRI is more useful in language-lateralization tasks, however, the role of fMRI in memory tasks in patients with epilepsy is still in research [53].

• **Positron Emission Tomography:** in around 70% to 90% of patients, 18F-FDG-PET proved to be helpful for the identification of epileptogenic temporal lobe in a study of Kim et al. in 2003. In a study done by Wong et al in 2010 found that hypometabolism detected by 18F-FDG-PET is typically larger than the presumed EZ and sometimes extends to remote extratemporal regions anatomically connected with mesial temporal structures [54].

• **Single Photon Emission Computed Tomography, SPECT:** it is a noninvasive method helpful to lateralize complex partial seizures in patients with drug-resistant MTLE. Functional hemodynamic changes in the epileptogenic regions and in areas of seizure spread can be detected by Ictal SPECT. In focal epileptic seizures Nitric oxide observed to be the mediator of the vasodilation. The subtraction ictal SPECT and subtraction ictal SPECT coregistered to MRI (SISCOM), are the recent development of computer-aided methods of post-acquisition processing of ictal and interictal SPECT images [55,56,57].

• **Magnetoencephalography, MEG:** epileptic spikes can be localized by MEG. EEG records the extracellular electrical current which is subject to distortion by different intervening tissues. MEG detects magnetic fields generated by neurons in the walls of cortical sulci. These neurons produce current dipoles tangential to the skull. However, currents produced by neurons at the tip of the gyri that are radial to the skull do not influence MEG. The intervening tissues can distort

the electrical currents produced in the sulci and gyri when recorded by EEG. However, MEG can easily record magnetic fields without distortion by different tissues such as bone, muscle, and skin. In addition, MEG measurements are absolute with MEG could help to reduce the need for invasive monitoring in focal epilepsy [39].

1.24. Treatment of MTLE

Among the focal epilepsies, Mesial temporal lobe epilepsy (MTLE) is the most common epilepsy which is pharmacoresistant. Surgical treatment and respective surgery are best for patients with intractable seizures due to unilateral MTLE [58]. For all cases of MTLE associated with hippocampal sclerosis, antiepileptic drugs are the first-line treatment for MTLE (MTLE/HS). But when they are not effective surgical management is done which includes:

• **Resective Surgery:** which includes selective amygdalohippocampectomy (SAH), that are, Transylvanian, subtemporal, and transcortical, or to anterior temporal lobectomy (ATL). Nowadays, a standard treatment for MTLE has become temporal lobe surgery because of a good outcome. Therefore these should be hypometabolism detected by 18F-FDG-PET is typically larger than the presumed EZ and sometimes extends to remote extratemporal regions anatomically connected with mesial temporal structures [54].

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2. Materials and Methods

This study titled "ROLE OF MAGNETIC RESONANCE IMAGING IN MESIAL TEMPORAL LOBE EPILEPSY WITH SPECIAL REFERENCE TO HIPPOCAMPAL VOLUMETRY AND T2 RELAXOMETRY" was conducted at Assam Medical College & Hospital, Dibrugarh over a Period of one year from 1st July 2018 to 30th June 2019.

- **Place of Study :** Department of Radio-diagnosis, AMCH, Dibrugarh.

- **Duration of Study :** One year

- **Type of Study :** Hospital-based case-control study

- **Study Group :** The study comprised of patients referred to the Department of Radiodiagnosis, AMCH, Dibrugarh from Neurology and Medicine department.

Case : include MTLE patients presented with history of seizure and positive EEG Findings.

- **Controls :** Include patients with normal EEG and MRI brain. o All cases were correlated with EEG findings for lateralization of the epileptic focus.

• Inclusion Criteria for Cases

Patients of all age groups with a clinical suspicion of mesial temporal lobe epilepsy.

• Exclusion Criteria for Cases

Infants.

Patients who did not give consent and were uncooperative. Epilepsy due to other causes like intracranial space-occupying lesions (SOLs), meningoencephalitis, granulomatous and demyelinating diseases.

• Inclusion Criteria for Controls

Patients of all age groups with normal EEG and MRI brain.

• Exclusion Criteria for Controls

Infants.

Patients who did not give consent and were uncooperative.

Patients with any neurological symptoms.

2.1. Sample Size

All consecutive cases of MTLE patients came to the radiology department fulfilling the inclusion and exclusion criteria during the study period. Controls were taken in the ratio of 1:1.

2.2. Ethical Clearance

Approval from the Institutional Ethics Committee (H) was obtained before conducting the study.

2.3. Study Protocol

The scheme was start with the patient's serial number, name,

age, address, hospital/ MRD number, date of admission and examination. A thorough case history including the clinical examination with symptoms, duration of symptoms, etc. Then these patients were subjected to MRI (SIEMENS MAGNETOM AVANTO 1.5 TESLA whole-body MRI SYSTEM)

- **Techniques:** Magnetic resonance imaging evaluation-MRI was performed on a 1.5 TESLA SIEMENS MAGNETOM AVANTO system. The following images were obtained in the temporal lobe protocol:

- **Axial and Sagittal T1WFSE:** TR=550 ms, TE=8.4 ms, Bandwidth=150, Slice thickness=5 mm.

- **Axial and Sagittal T2W FSE:** TR=3800 ms, TE= 90 ms, Bandwidth =190, Slice thickness=5 mm.

- **Axial FLAIR:** TR=9020 ms, TE=87 ms, T1=2502.3 ms, Slice thickness=5mm.

- **Coronal Oblique Fast FLAIR Images:** (TR/TE/TI 9020/87/2502.3, 3mm thick with 1.5 mm gap).

The coronal images were acquired perpendicular to the long axis of the hippocampus, defined by the sagittal images.

- **Coronal Oblique T2 FSE Images:** (TR/TE/TI 4500/84/1, 3 mm thick with 1.5 mm gap)

- **Oblique Coronal 3D T1 Inversion Recovery Images:** (TR/TE/TI 30/7/1, 1.5 mm thick).

- **Volumetric Analysis.** An oblique coronal FLAIR sequence (TR: 9020, TE: 87, Patients who did not give consent and were uncooperative. Patients with any neurological symptoms.

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2.7. Statistical Analysis

Continuous variables were described using mean and SD, and categorical variables were described using frequency and percentage. The sensitivity of the MRI scan was obtained.

The study was conducted after obtaining clearance from the Institutional Ethics Committee (Human), Assam Medical College & Hospital, Dibrugarh.

Statistical analysis was performed using SPSS-16 software.

3. Results and Observations

The present study consisted of 40 cases of MTLE presenting with a history of seizure and positive EEG Findings on whom MRI was performed with specific Epilepsy protocol in the Department of Radiodiagnosis, Assam Medical College & Hospital, Dibrugarh, during the period from 1st July 2018 to 30th June 2019.

The study was carried out to detect architectural changes of the hippocampus by MRI with evaluation of T2 relaxation time and hippocampal volume in patients with mesial temporal sclerosis.

The results had been summarized and presented in tabular forms under different headings:

AGE GROUP (<i>in years</i>)	CASE		CONTROL	
	<i>n</i>	%	<i>n</i>	%
<10	15	37.50	8	20.00
11—20	6	15.00	9	22.50
21—30	4	10.00	11	27.50
31—40	7	17.50	7	17.50
41—50	6	15.00	5	12.50
> 50	2	5.00	0	0.00
TOTAL	40	100.00	40	100.00
MEAN ± S.D.	30.40 ± 18.01 <i>years</i>		31.48 ± 15.18 <i>years</i>	
<i>p value</i>	0.77364			

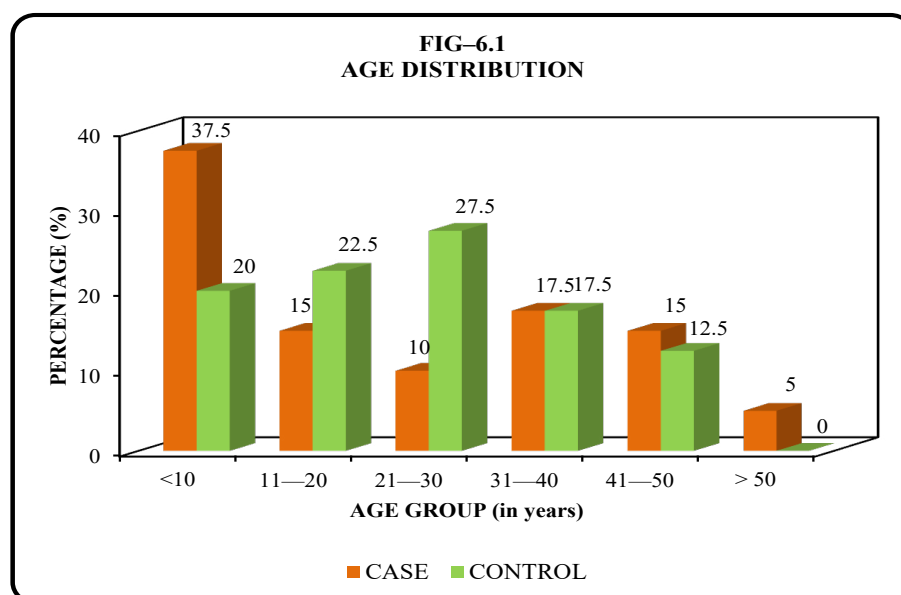


Table 1: Age Distribution

From Table-1, the mean of age distribution was 31.48 ± 15.18 years in the control group. There was no subject in the >50 years range in control group. The mean age in the cases group was 30.40 ± 18.01 years. The maximum number

of patients were in two age group ranges <10 years and 31-40 years. The age group matches near about same for control and cases.

SEX	CASE		CONTROL	
	<i>N</i>	%	<i>n</i>	%
Male	24	60.00	24	60.00
Female	16	40.00	16	40.00
TOTAL	40	100.00	40	100.00
RATIO (Male : Female)	1.5 : 1		1.5 : 1	

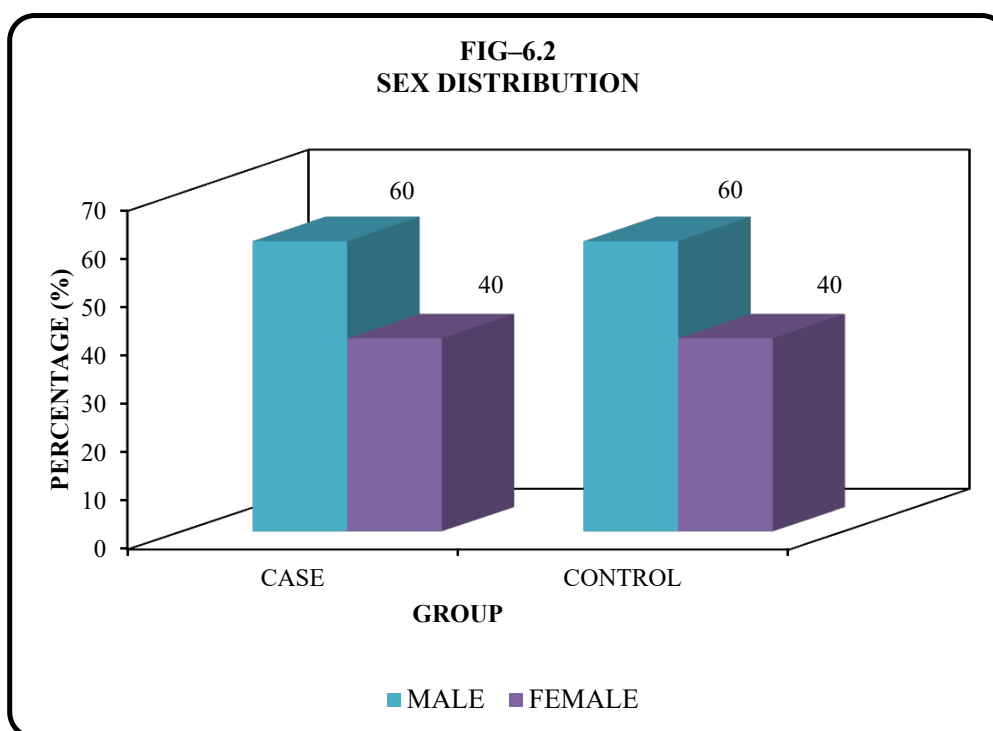


Table 2: Sex Distribution

From Table-2, the male to female ratio was 1.5: 1 showing mild male predominance but no significant difference in male and female ratio.

AGE OF ONSET (in years)	NUMBER (n)	PERCENTAGE (%)
0—10	12	30.00
11—20	15	37.50
20—30	6	15.00
>30	7	17.50
TOTAL	40	100.00
MEAN $\pm$ S.D.	17.48 $\pm$ 11.31 years	

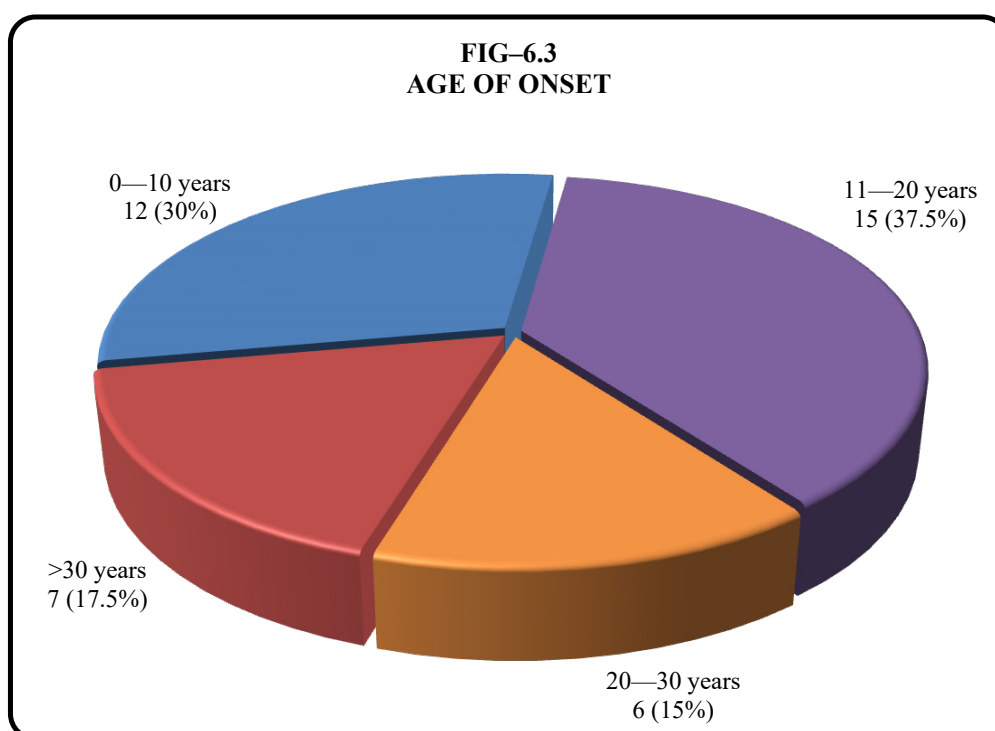


Table 3: Age of Onset of Seizures

Table-3 showed that most of the patients had seizure onset in the second decade of life with a mean age of seizure onset being 17.48 ± 11.31 years. 30% had seizure onset below 10 years, 17.5 % in more than 30 years and 15% in 20-30 years of age group.

DURATION	NUMBER (n)	PERCENTAGE (%)
6—12 months	0	0.00
1—6 years	12	30.00
7—12 years	9	22.50
13—20 years or above	19	47.50
TOTAL	40	100.00
Mean $\pm$ S.D.	12.92 $\pm$ 8.67 years	

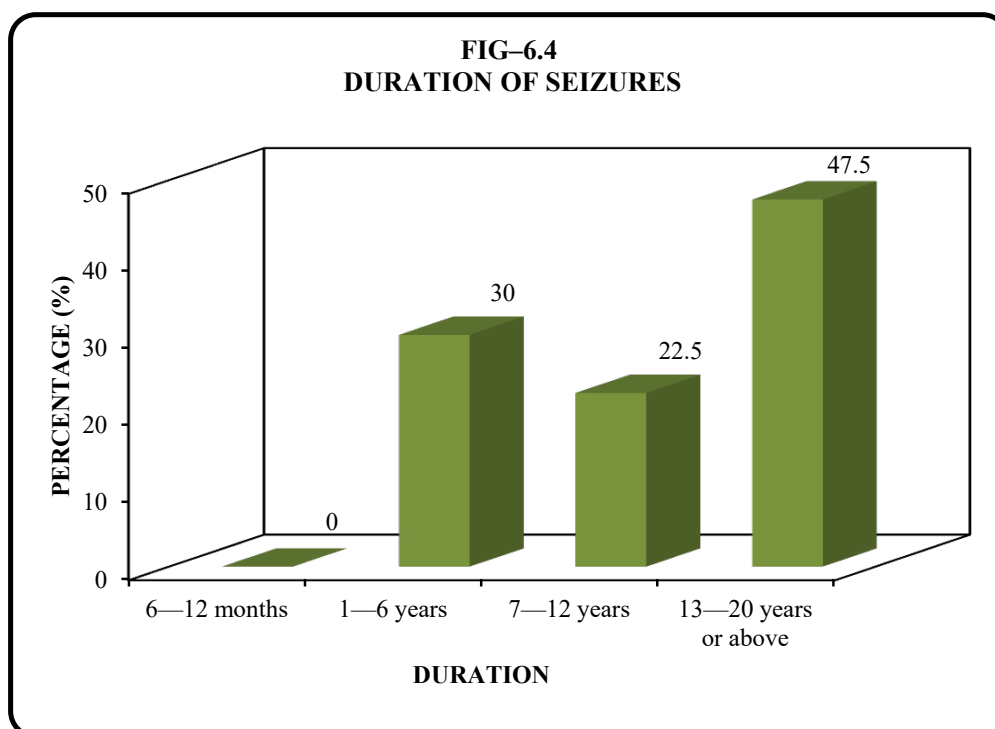


Table 4: Duration of Seizures

The duration of seizures ranged from 1 year to 35 years and a mean duration of seizures was 12.92 ± 8.67 years according to table 4. No patient was there in duration range of 6 months-12 months.

FEATURES	NUMBER (n = 40)	PERCENTAGE (%)
Hippocampal atrophy	25	62.50
T2/FLAIR hyperintensity	22	55.00
Loss of internal architecture and hippocampal head digitations	17	42.50
Thinning of the collateral white matter of Parahippocampal gyrus	16	40.00
Dilatation of temporal horn	19	47.50
Temporal lobe atrophy	7	17.50
Fornix atrophy	6	15.00
Mamillary body atrophy	7	17.50
Thalamic atrophy	3	7.50

FIG-6.5
FEATURES OF CONVENTIONAL MRI

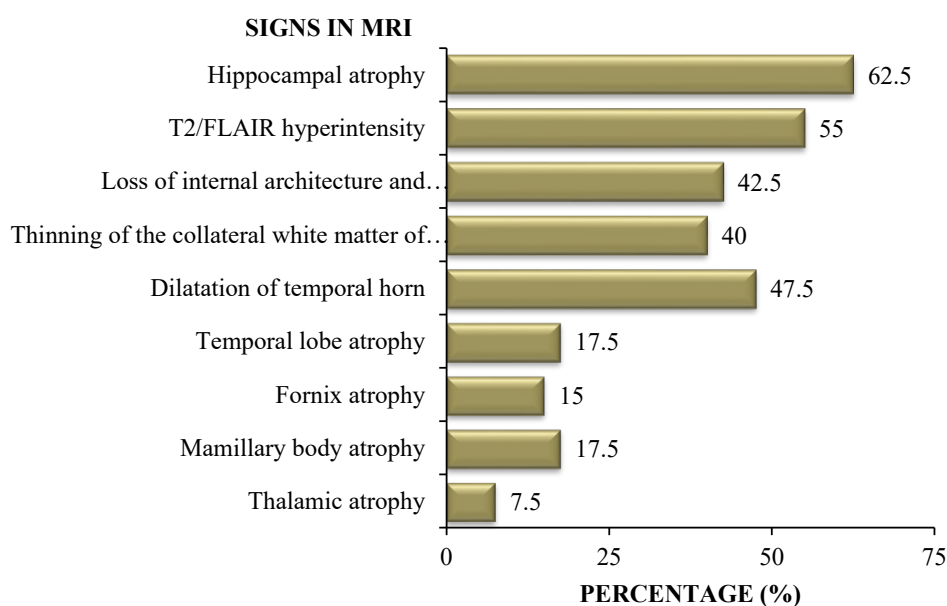


Table 5: Features of Conventional MRI

Table-5 showed that hippocampal atrophy (25 out of 40 cases) and T2/FLAIR hyperintensity (22 out of 40) were most commonly identified features in mesial temporal sclerosis, followed by dilatation of temporal horn, loss of hippocampal internal architecture & head digitations and thinning of

collateral white matter in parahippocampal white matter. Of the extratemporal changes, Mammillary body atrophy was most commonly seen in 7 patients followed by fornix atrophy and 3 cases of thalamic atrophy.

LATERALITY	NUMBER (n = 40)	PERCENTAGE (%)
Unilateral:		
♦ Right	13	32.50
♦ Left	18	45.00
Bilateral	7	17.50

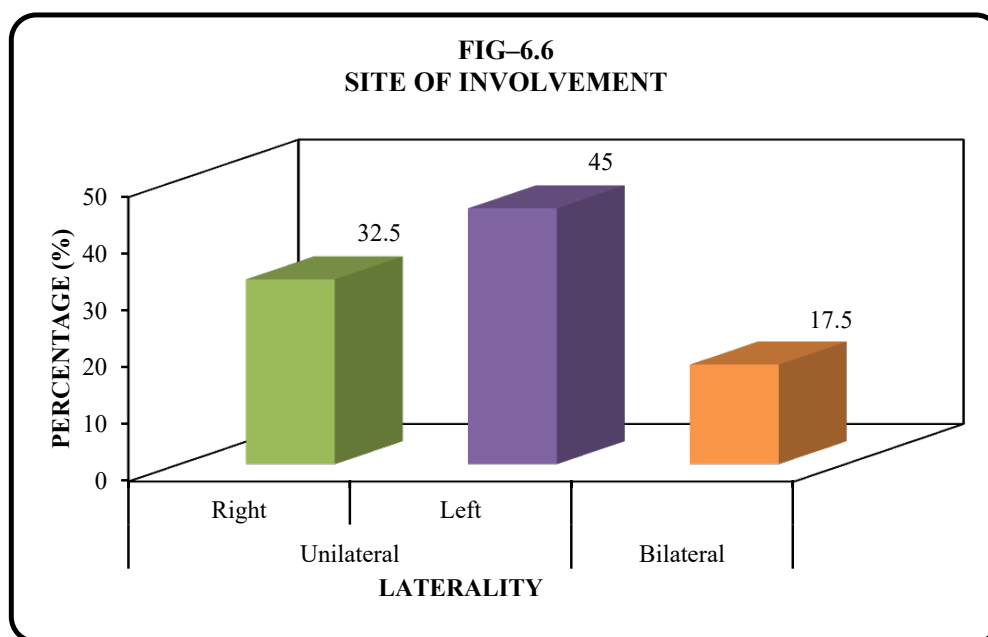


Table 6: Site of Involvement

Table-6 showed that 13 out of 40 cases involved the right hippocampus, 18 out of 40 cases involved left hippocampus and 7 cases had asymmetrical bilateral hippocampi involvement. We had taken controls for the study which constituted 40 patients; 24 males and 16 females without any neurological or psychiatric complain and all had normal MRI brain and scanned at Siemens Avanto 1.5T machine. The group was randomly selected. They were evaluated

with conventional MR sequences along with coronal flair, thin section T1 inversion recovery and 16 gradient-echo images. T2 relaxation time was obtained for right and left hippocampus and normal range of T2 relaxation time was assigned for our MRI machine. Simultaneously, hippocampal volume was calculated for the right and left hippocampus and the normal range of hippocampal volume was assigned for our study.

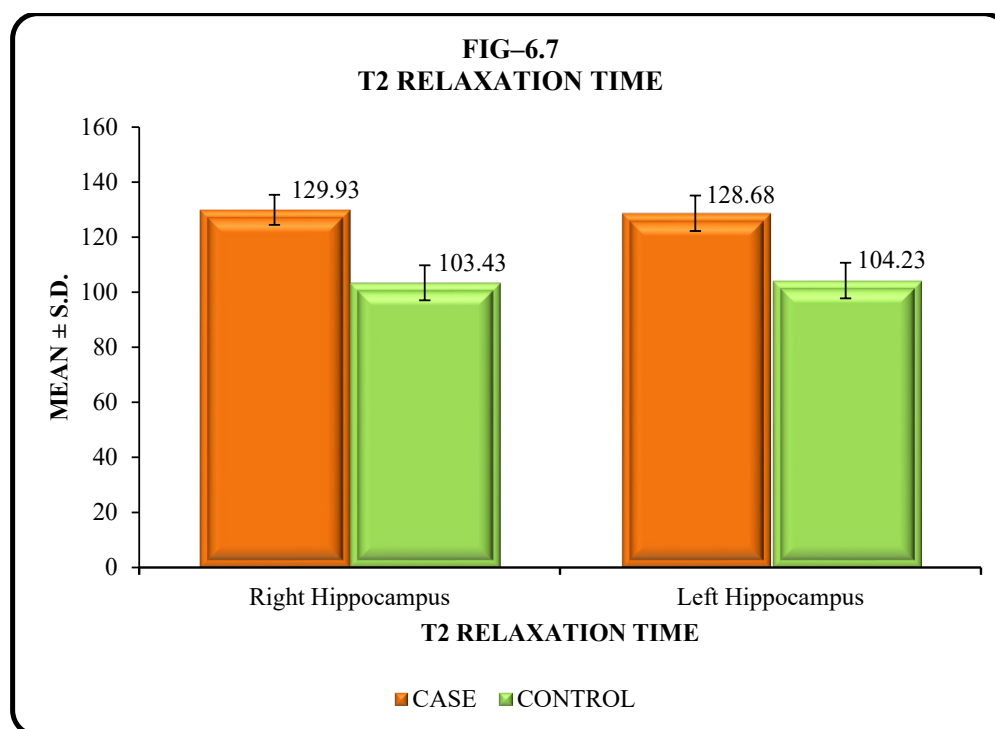
T2 RELAXATION TIME	CASE			CONTROL			p value
	Number (n)	Mean	± S.D.	Number (n)	Mean	± S.D.	
Right Hippocampus	16	130.1*	7.69	40	103.33	6.6	<0.001
Left Hippocampus	21	128.17*	5.83	40	104.35	6.36	<0.001

*Mean values of all the abnormal T2 Relaxation Time

Table 7: T2 Relaxation Time

In the control group mean T2 relaxation value was 103.33 ms for the right hippocampus and 104.35 ms for the left hippocampus. A value 2 SD above the mean (116.5 and

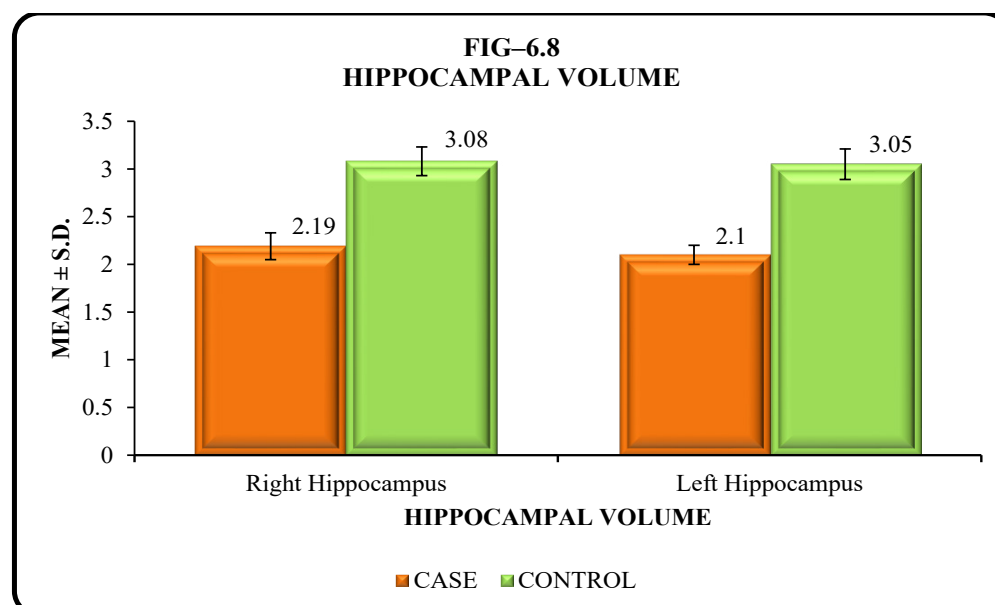
117.07 ms for right and left respectively) was taken as cut off value for normal T2 relaxation for our machine.



In cases, according to table 6.7, we found, mean T2 relaxation value in the right and left abnormal hippocampi were 130.1 ms and 128.17 ms respectively. As P values were less than 0.0001, so the values were statistically highly significant.

HIPPOCAMPAL VOLUME	CASE			CONTROL			p value
	Number (n)	Mean	± S.D.	Number (n)	Mean	± S.D.	
Right Hippocampus	24	2.19*	0.14	40	3.08	0.15	<0.001
Left Hippocampus	29	2.10*	0.10	40	3.05	0.16	<0.001

*Mean values of all abnormal hippocampal volume of affected side



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Table 8: Hippocampal Volume

Similar to T2 relaxometry the average hippocampal volume was 3.08 cc for the right hippocampus and 3.05 for the left hippocampus in control patients. A value 2 SD below the mean (2.78 cc and 2.72 cc for right and left respectively) was taken as cut off value for normal hippocampal volume

for our study. In cases according to table 6.8, we found, mean hippocampal volume in the right 24 and left 29 abnormal hippocampi were 2.19 ± 0.14 cc and 2.10 ± 0.10 cc respectively. As P values were less than 0.0001, so the values were statistically highly significant.

HIPPOCAMPAL VOLUME	CASE			CONTROL			<i>p value</i>
	<i>Number (n)</i>	<i>Mean</i>	<i>± S.D.</i>	<i>Number (n)</i>	<i>Mean</i>	<i>± S.D.</i>	
Hippocampal Volume Difference	29	0.98	0.20	40	0.15	0.08	<0.001
Hippocampal Volume Ratio	29	0.69	0.05	40	0.95	0.02	<0.001

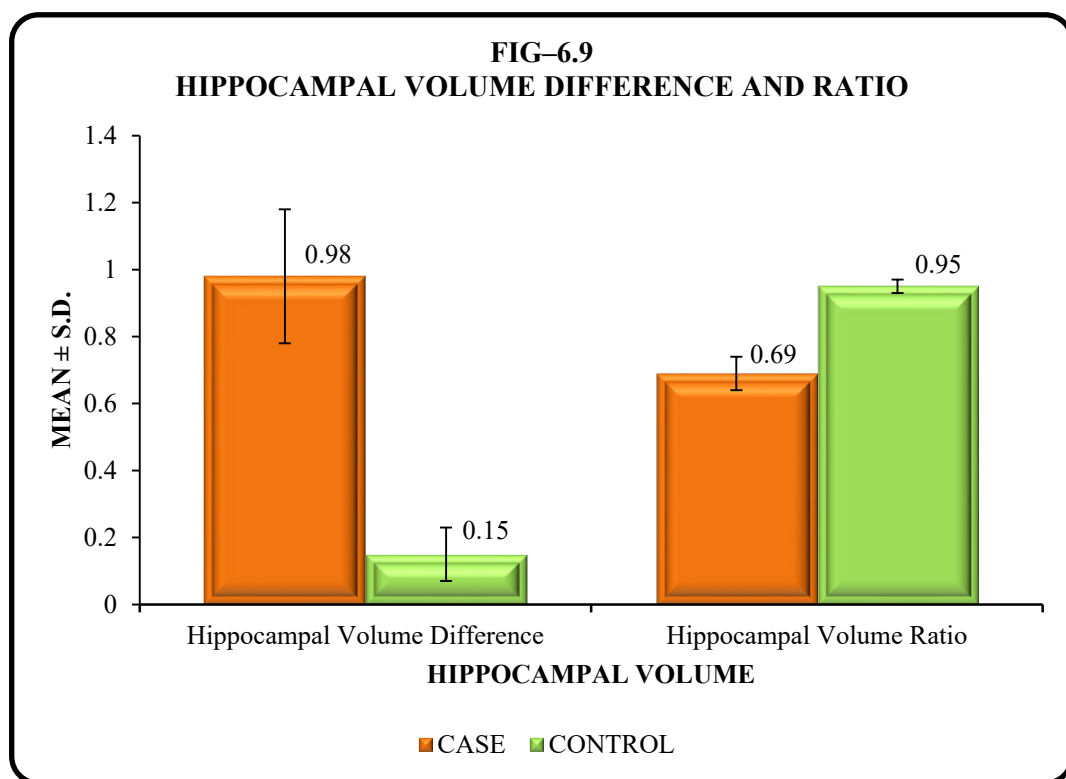


Table 9: Hippocampal Volume Difference and Ratio

We also calculated hippocampal volume difference and hippocampal volume ratio found as 0.15 cc and 0.95 respectively in the control group. A value 2 SD above the mean of HVD (0.3 cc) and 2SD below the mean of HVR (0.91)

was taken as a cut-off to diagnose all the unilateral cases of MTLE. By this we were able to detect 29 unilateral cases of MTLE.

MODALITY	NUMBER (n)	PERCENTAGE (%)
Conventional MRI	27	67.50
MRI with T2 Relaxometry	31	77.50
MRI with Hippocampal Volumetry	35	87.50
MRI with Hippocampal Volumetry + T2 RELaxometry	38	95.00

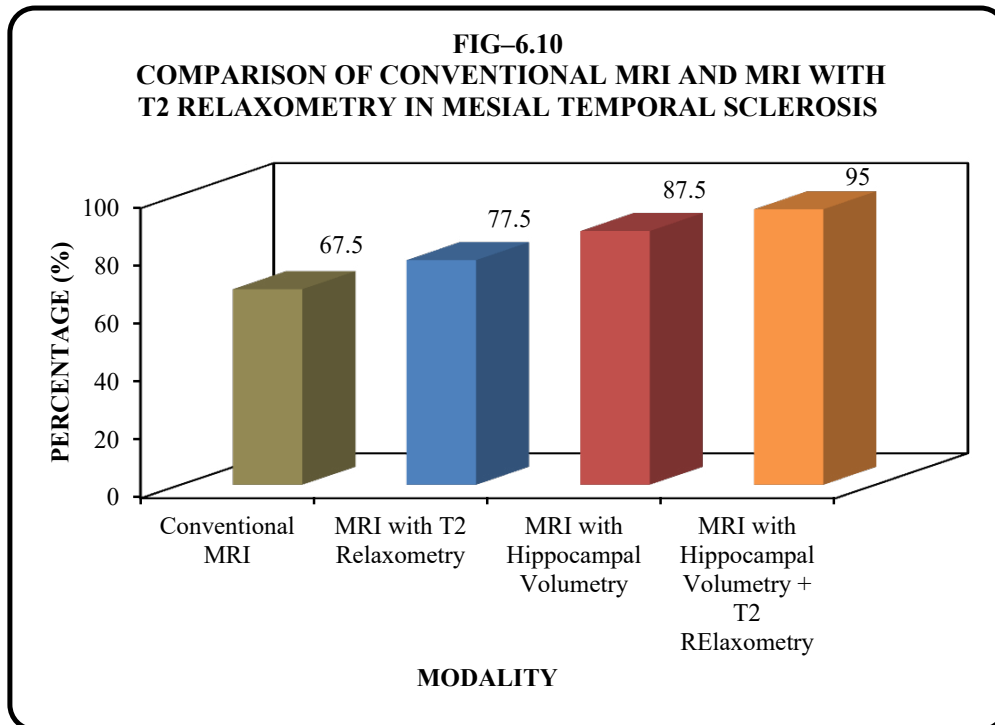


Table 10: Comparison of Conventional MRI, MRI with T2 Relaxometry, Hippocampal Volumetry and Combined Modality in Mesial Temporal Sclerosis Detection

Table-10 showed comparison of conventional MRI, MRI with T2 relaxometry, hippocampal volumetry and combined modality of all three approaches with respect to interictal scalp EEG which was gold standard in our study for detection of mesial temporal lobe sclerosis. Conventional MRI was able to detect only 27 cases of MTLE. MRI combined with T2 relaxometry was able to detect 31 cases of suspected mesial temporal sclerosis. MRI combined with hippocampal volumetry detected 35 cases. However, MRI combined with both T2 relaxometry and hippocampal volumetry was able to detect the highest number of MTLE cases, 38. Therefore, the total sensitivity of MRI combined with both T2 relaxometry and hippocampal volumetry was 95% for the detection of MTLE.

4. Discussion

The presents study on 40 suspected cases of MTLE with positive EEG findings and on 40 patients taken as control irrespective of age and sex was done for a period of one

year in the Department of Radiodiagnosis, Assam Medical College & Hospital, Dibrugarh. All the subjects included underwent MRI with special epilepsy protocol in which an evaluation of right and left hippocampal T2 relaxation time and hippocampal volume was done. Controls were used to get the normal cut-off of T2 relaxometry and hippocampal volume for the cases. EEG findings were taken as gold standard and sensitivity of Conventional MRI, MRI with T2 relaxometry, MRI with hippocampal volumetry and MRI with both T2 relaxometry and hippocampal volumetry were determined.

4.1. The Findings were as Follows

4.1.1 Age Distribution

Among 40 patients included in our study, the mean age of distribution was 30.40 ± 18.01 years. However, the maximum number of patients recruited in our study, 15 were in the age group of < 10 years which constitutes 37.5 %. Another larger group was of 31-40 years which included 7 patients

(17.50%). In resemblance to our study, Abdel Aziz Kamal Aun found 32 years as average age of patients distribution, in their study of 30 patients [73]. Maria Teresa Castilho Garcia Santana found the mean age of presentation 35 years in their study of 120 patients with TLE-MTS and 50 controls [64,67].

4.1.2. Sex Distribution

In our study of 40 patients, 24 patients were male and 16 were female giving males: female ratio of 1.5:1 which suggested no significant difference in MTLE distribution on the basis of sex. Other studies like done by Abdel Aziz Kamal Aun, Livia Conz and M. Garcí'a-Fin~ ana also not shown sex variation in the distribution of MTLE [73-75].

4.1.3. Age of Seizure Onset

15 cases (37.5%) showed seizure onset in the age group range of 11-20 years, followed by 12 cases (30%) in age group of 0-10 years, 7 (17.50%) in age group of >30 years and least 6 cases (15%) in age group range of 20-30 years [68-70]. Therefore, we got our mean age of seizure onset of 17.48 ± 11.31 years. A.C. Coan in their study of 33 patients found the median age of onset of 12.3 years, which was in concordance with our study median age of seizure onset, 16.5 years [71-75]. Similar results were found by Simon P C Bower in their study where the mean age of seizure onset was 11.5 years [76]. Another study of Kousuke Kanemoto found 14.7 years as the mean age of seizure onset [77].

4.1.4. Seizure Duration

About 47.50% (19 cases) of patients in our study were found to have seizure duration ranged from 13 to 20 years, 30 % (12 cases) of patients were in the range of 1-6 years and 22.50% (9 cases) in range of 7-12 years. No patient was found in the range of 6-12 months. According to the data, our mean range of duration of seizures came to be 12.92 ± 8.67 years. These findings were correlatable with the study of Adam P. Smith in which the mean duration of the seizure disorder was 13.4 years and Kousuke Kanemoto where they found the mean duration of seizure of 14 years [77,78].

4.2. Conventional MRI Features of Mesial Temporal Sclerosis

Conventional MRI findings that were found in MTLE cases were broadly divided into two types primary and secondary findings as described in the text. The primary findings which include hippocampal atrophy and T2/FLAIR hippocampal hyperintensity were found in 62.50 % (25 cases) and 55 % (22 cases) of patients respectively. These findings resembled with study of E. Kobayashi et al (2004) where T2 hippocampal signal abnormalities were found in 79 (52%) subjects and Hippocampal atrophy was found in 90 (59%) individuals and another study of Paramdeep Singh et al (2013) where they found increased signal on T2w in 50% AGE OF SEIZURE ONSET: 15 cases (37.5%) showed seizure onset in the age group range of 11-20 years, followed by 12 cases (30%) in age group of 0-10 years, 7 (17.50%) in age group of >30 years and least 6 cases (15%) in age group range of 20-30 years [79]. Therefore, we got our mean age of seizure onset of 17.48 ± 11.31 years. A.C. Coan in their study of 33 patients

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About 47.50% (19 cases) of patients in our study were found to have seizure duration ranged from 13 to 20 years, 30 % (12 cases) of patients were in the range of 1-6 years and 22.50% (9 cases) in range of 7-12 years. No patient was found in the range of 6-12 months [60-64]. According to the data, our mean range of duration of seizures came to be 12.92 ± 8.67 years. These findings were correlatable with the study of Adam P. Smith (2011) in which the mean duration of the seizure disorder was 13.4 years and Kousuke Kanemoto (1998) where they found the mean duration of seizure of 14 years [77,78].

4.5. Conventional MRI Features OF Mesial Temporal Sclerosis

Conventional MRI findings that were found in MTLE cases were broadly divided into two types primary and secondary findings as described in the text. The primary findings which include hippocampal atrophy and T2/FLAIR hippocampal hyperintensity were found in 62.50 % (25 cases) and 55 % (22 cases) of patients respectively. These findings resembled with study of E. Kobayashi (2004) where T2 hippocampal signal abnormalities were found in 79 (52%) subjects and Hippocampal atrophy was found in 90 (59%) individuals and another study of Paramdeep Singh (2013) where they found increased signal on T2w in 50% Another study of L Bonilha (2003) on 25 patients with drug-refractory MTLE found hippocampal Volume Of Right And Left Side was 1764 and 1823 in cases and 3260 and 3279 in controls respectively [79,80,81].

4.6. Hippocampal Volume Ratio and Hippocampal Difference

Two new parameters were included in our study in which one was hippocampal volume ratio which was calculated by division of smaller to larger hippocampal volumes. In the control group, value of HVR ranged from 0.92 to 0.99, and from these mean was calculated and value $<2SD$ of mean was taken as cut-off (<0.91) for diagnosis of unilateral hippocampal atrophy. Another parameter was HVD which was calculated by subtracting right-left hippocampal volume and the mean of HVD in controls was found to be 0.15 ± 0.08 cm³ (0.03–0.26 cc). All the values which fall outside the $>2SD$ upper limit of the range (0.3 cc) were considered abnormal. Using this criterion, we were able to detect 29 out of 35 (82.9%) TLE patients who had HVD of more than 0.3 cc and HVR less than 0.91. The rest of the 6 patients had bitemporal abnormalities which were detected by EEG and quantitative methods of MRI studied, hippocampal volumetry or T2 relaxometry. These findings were in resemblance to the study of Paramdeep Singh (2013) [45].

4.7. Comparison of Qualitative and Quantitative Assessments

After combing all the primary and secondary findings of conventional MRI we were able to detect a total of 27 cases out of 40 cases. Giving sensitivity of conventional MRI alone of 67.50 %. A study which was familiar was by Abdel Aziz Kamal Aun (2015) where they were able to detect 60% cases by conventional MRI [73]. and another study of Paramdeep Singh (2013) where 65% sensitivity was found in concordance with EEG [45]. We were able to detect 4 more cases of MTLE by using T2 relaxometry. In all we were able to detect 31 cases out of a total of 40 cases of MTLE, giving the sensitivity of T2 relaxometry in concordance with EEG as 77.50%. This was relatable with Paramdeep Singh (2013) study where by T2 relaxometry 14 cases were detected out of 20 cases of MTLE, giving the sensitivity of T2 relaxometry 70% in concordance to EEG [45]. Then the last parameter we had used was hippocampal volumetry by which 8 more cases were detected which did not show any findings on conventional MRI and 7 more cases which were

negative on T2 relaxometry out of which most of them were bilaterally affected MTLE [59]. However, 3 cases detected by T2 relaxometry were negative on hippocampal volumetry.

Hippocampal volumetry in all was able to detect 35 cases of MTLE, giving its sensitivity of 87.50%. Similar results were found in Paramdeep Singh (2013) where they found the sensitivity of hippocampal volumetry alone was 75%. In all on combining all MRI quantitative and qualitative parameters, we were able to detect 38 cases out of 40 cases and 2 cases were MRI negative [45]. So, on combining sensitivity becomed 95 %. A study of Nikdokht Farid (2012) revealed that quantitative MR imaging depicted HA in patients at rates that may exceed those based on visual inspection of the clinical MR imaging study (88% vs 76%) [65,66]. Then the last parameter we had used was hippocampal volumetry by which 8 more cases were detected which did not show any findings on conventional MRI and 7 more cases which were negative on T2 relaxometry out of which most of them were bilaterally affected MTLE. However, 3 cases detected by T2 relaxometry were negative on hippocampal volumetry. Hippocampal volumetry in all was able to detect 35 cases of MTLE, giving its sensitivity of 87.50%. Similar results were found in Paramdeep Singh (2013) where they found the sensitivity of hippocampal volumetry alone was 75%. In all on combining all MRI quantitative and qualitative parameters, we were able to detect 38 cases out of 40 cases and 2 cases were MRI negative [45,46]. So, on combining sensitivity becomed 95 %. A study of Nikdokht Farid (2012) revealed that quantitative MR imaging depicted HA in patients at rates that may exceed those based on visual inspection of the clinical MR imaging study (88% vs 76%) [47,48,65].

5. Conclusion

In adults, the most common form of epilepsy was Mesial temporal lobe epilepsy (MTLE). There were several pathologic causes of MTLE, among them hippocampal sclerosis (HS) was the main cause. MRI findings and histological findings were normal in some of the patients. Although combination of clinical and MRI information with the EEG findings was most useful in identifying the seizure focus for surgical treatment of mesial temporal lobe epilepsy. In our study, we found no gender difference and MTLE was more prevalent in the adult age group. Lesions were more widespread in the left hemisphere. In conventional MRI primary and secondary features can be seen to detect MTS. Hippocampal atrophy was the most common and T2/FLAIR hyperintensity was the second most common primary sign of MTS in our study. Secondary MR findings seen in mesial temporal sclerosis gave suspicion in mild cases and in bilateral cases, increasing the sensitivity; however, they were not sensitive predictors of this entity by themselves.

Hippocampal volume measured in the control group can be used as normative data that would be applicable to the management of Indian patients with medically refractory epilepsy. Right and left hippocampal volumes were positively correlated, and the right hippocampal volume was larger

than left by a statistically insignificant amount. No significant correlation of hippocampal volumes and T2 relaxation times existed with gender or age. Patients with intractable temporal lobe epilepsy had smaller mean hippocampal volume and longer T2 relaxation time ipsilateral to seizure focus. Hippocampal volumes and T2 values correlated inversely with each other in TLE cases. HVR and HVD were the new two parameters that were diagnostic of unilateral MTS. There was an increase in the sensitivity of detection of MTS in epilepsy patients on including Quantitative methods like T2 relaxometry and Hippocampal volumetry with conventional MRI. Especially these were more sensitive in diagnosing bilateral pathologies and mild unilateral pathology. Among all modalities tested in our study, hippocampal volumetry proved to be most sensitive giving 87.5% lateralization. Hippocampal volumetry and T2 Relaxometry are the quantification methods which are easily available nowadays. Therefore can be used routinely for detection of MTLE cases. Other new modalities are in research for the detection of MTS not used commonly like MRS, Diffusion MR, Perfusion MRI, Functional MRI, etc. However, confirmative or specific diagnostic modality is always pathological diagnosis by HPE after surgery of the patient.

Summary

During the period from 1st July 2018 to 30th June 2019, this present study was conducted in the Department of Radiodiagnosis, Assam Medical College and Hospital, Dibrugarh, Assam. 40 patients with clinically suspected cases of MTLE and positive EEG findings were studied irrespective of age and sex. In all cases, a brief history was taken which was followed by clinical examination of the patients according to the planned proforma. The patients then underwent MRI with special planned epilepsy protocol including hippocampal volumetry and T2 relaxometry. Another 40 subjects were taken who had normal MRI Brain. Mean T2 relaxation time was obtained for both hippocampi and these values were used to standardize the normal range for our machine. Mean Hippocampal volumes were also calculated for right and left hippocampi, to used as cut off for our cases. Taking EEG as the gold standard, the diagnostic performance of Conventional MRI, T2 relaxometry and Hippocampal volumetry were calculated. We categorized the cases as conventional MR positive, T2 relaxometry MR positive, Hippocampal volumetry MR positive and MR negative MTLE. Out of 40 cases studied we found 27 cases were conventional MR positive, 31 cases were T2 relaxometry positive and 35 cases were Hippocampal volumetry positive and 2 cases were MR negative MTLE.

Following Findings were Found in the Study

- 95% of patients recruited in the case group of our study, were below 50 years of age, only 2 cases were above 50 years with a mean age of distribution of 30.40 ± 18.01 years. In the control group, all the cases were below 50 years with a mean age of 31.48 ± 15.18 years.
- No significant difference in sex distribution was noted. Male: female ratio was 1.5:1.

- In our study most of the cases had onset of seizures below 20 years of age, that was near about 67.5 %, another 15% had onset of seizures in 20-30 years of age and remaining 17.5 % had onset of seizures in > 30 years of age. We found the mean age of onset of seizures was 17.48 ± 11.31 years.
- The mean duration of seizures found in our study was 12.92 ± 8.67 years with 47.5% of cases had a duration of seizures >13 years. There was no patient found having a duration of seizure in range of 6-12 months.
- In convention MRI, the most common finding, we found was hippocampal atrophy in 62.5% of cases and 2nd most common finding was T2/FLAIR hyperintensity present in 55% of cases. These two were the primary and most common findings of MTLE on MRI.
- In secondary MRI signs of MTLE, most common was dilatation of temporal horn found in 47.50% cases, followed by loss of internal architecture and hippocampal head digitations in 42.50% cases and less common was thinning of collateral white matter of para-hippocampal gyrus in 40% cases,
- Among the extratemporal signs of mesial temporal sclerosis, 17.5% cases showed atrophy of temporal lobe and mamillary body, fornix atrophy present in 15% cases and least common finding was thalamic atrophy which was present in 7.5 % cases.
- By conventional MRI 27 cases were detected MR positive for MTLE. Thus its sensitivity was 67.5% in the detection of MTLE.
- In our study, left-sided MTLE cases were more that were 18 in number compared to right-sided MTLE and bilateral cases which were 13 and 7 in number respectively.
- Mean T2 relaxation time evaluated by 16 echo sequences in the control group for standardization was 103.43 ± 6.35 ms in the right hippocampus and 104.23 ± 6.47 ms in the left hippocampus. Cut of value was taken 2SD above the mean value and was set at 116.5 ms and 117.07 ms for the right and left respectively for our machine.
- Taking into consideration the above cut-off values, 16 cases were detected abnormal on right side and 21 cases were abnormal on the left side which had T2 relaxation time more than the normal T2 relaxation time. All the abnormal T2 relaxation times were evaluated and mean was obtained for both right and left hippocampus which came out to be 130.10 ± 7.69 ms and 128.17 ± 5.83 ms respectively in our MTLE cases.
- By using T2 relaxometry, quantitative method 4 extra cases were detected which were negative on conventional MRI, making a total of 31 cases and sensitivity of 77.50%.
- Another quantitative parameter we had included in our study was hippocampal volumetry, similar to that of T2 relaxometry hippocampal volume was detected in all control group subjects on both sides to make it as reference for normal individuals which came out to be 3.08 ± 0.15 cc and 3.05 ± 0.16 cc for right and left hippocampus respectively. Cut of value was taken 2SD below the mean value and was set at 2.78 cc for the right hippocampus and 2.72 cc for the left hippocampus.
- Taking the above-measured values as cut-off 24 cases showed atrophy in the right hippocampus and on left 29

cases showed atrophy. Mean hippocampal values calculated in cases for right and left hippocampus were 2.19 ± 0.14 cc and 2.10 ± 0.10 cc respectively.

- In all, 35 cases were detected as MTLE by using the Hippocampal volumetry parameter. Therefore, hippocampal volumetry increased the sensitivity of MRI to 87.5%.
- Two new parameters were included in our study namely, HVD and HVR which helped in the detection of unilateral cases of MTLE. Mean HVD and HVR were calculated from the control group which came out 0.15 ± 0.08 cc and 0.95 ± 0.02 respectively. On considering this, HVR of less than 0.91 (<2SD of the mean value) was considered to be diagnostic of unilateral hippocampal atrophy and similarly, HVD was considered abnormal when values fell outside the upper limit of the 2SD of the mean value calculated from control group (0.3 cc). Using these criteria, 29 cases out of 35 (82.85 %) TLE patients had a volume difference of more than 0.3 cc and HVR of less than 0.91. The rest of the 6 patients had bitemporal abnormalities which were detected by EEG and quantitative methods of MRI studied, hippocampal volumetry or T2 relaxometry.
- On including both the quantitative and qualitative methods of detection in our study we were able to detect total of 38 cases of MTLE. Therefore, sensitivity calculated was 95% which was more in comparison to the individually use of conventional MR, T2 relaxometry or hippocampal volumetry. However, 2 cases were present in our study which didn't show any sign of MTLE on MRI called MR negative MTLE cases which were positive on EEG.

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