**University of Khartoum**

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# THE CLINICAL, ELECTROENCEPHALOGRAPHIC AND MRI FINDINGS IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

By

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# Dedication

To my husband, who had helped me a lot , to
my brother Hafiz , to my family and to my parents.

# Acknowledgments

It is with great pleasure that I record my gratitude to my supervisor Dr: Abbashar Hussein.

I wish to thank him for his meticulous supervision, encouragement and patience.

My debt to him is so great.

Also I would like to extend my gratitude to Dr.Amar Eltahir.

## ABBREVITIONS

| | |
|---|---|
| AEDs | Anti-Epileptic Drugs |
| CNS | Central Nervous System |
| CSF | Cerebro Spinal Fluid |
| CT | Computed Tomography |
| EEG | Electro Encephalo Gram |
| FDA | Food &Drug Adminstration |
| FLAIR | Fluid Attenuated Inversion Recovery |
| ILAE | International League Against Epilepsy |
| MRI | Magnetic Resonance Imaging |
| MTLE | Mesial Temporal Lobe Epilepsy |
| NDL | Neuroevelopmental Lesion |

| | |
|---|---|
| SPECT | Single Photon Emission Computed Tomography |
| SPGR | Spoiled Gradient Recall |
| SUDEP | Sudden Unexpected Death in Epilepsy |
| TLE | Temporal Lobe Epil |
| VNS | Vagus Nerve Stimulation |

# Abstract

A total of 33 patients with temporal lobe epilepsy who were seen in out patient clinics in Khartoum area in the period between June 2004-February 2005 were studied.

The aim of the study was to determine the clinical patterns, EEG &MRI findings of temporal lobe epilepsy among Sudanese patients.

The data were collected through a questionnaire containing detailed medical history, thorough physical examination and specific investigations including electroencephalogram and brain MRI.

The pattern was as follows:

Most of the study group population were between (16 – 30) years. However the age of onset was in childhood period. Males (54.5%) were more affected than females. Aura (87.9%) was common in patients with TLE .Most of patients had complex partial seizure & (33.3%)of patients had secondary generalization.(9.1%)had cranial nerves palsies ,(15.2%) had symptoms of increased intra-cranial pressure and (15.2%) had weakness.(15.2%)had past history of febrile convulsions.(9.1%)gave a past history of meningitis or encephalitis.(27.3%) gave a family history of epilepsy.Inter-ictal EEG was abnormal in (81.8%).MRI was abnormal in (27.3%), however hippocampal sclerosis was found in just (3.0%).

So we concluded that most of our study population were young adults .

TLE can affect both sexes. Here males were affected more than females. Aura was a common finding in patients with TLE.

Most of patients had complex partial seizure. Some of patients had secondary generalization. Presence of focal neurological symptoms & signs raise the possibility of structural abnormality. Febrile convulsions and central nervous system infection during childhood were risk factors for developing TLE.

Most of the study group had abnormalities in their inter-ictal EEG.

Small number of patients showed abnormalities in their MRI.

So ,we recommend to do a full clinical assessment ,EEG &brain MRI for all patients with TLE ,also to treat febrile convulsions in children to prevent TLE to occur in later life.

# ملخص الأطروحة

هذه دراسة وصفية أنية أجريت في العيادات المحولة في منطقة الخرطوم .حيث قمت بدراسة ثلاث وثلاثين حالة من المرضى الذين يعانون من صرع الفص الصدغي.تم جمع المعلومات عن طريق تعبئة استمارة استبيان شاملة على التاريخ المرضي والفحص السريري لكل حالة بالإضافة إلى إجراء الفحوصات المعملية الخاصة . وعمل تخطيط دماغي وصورة رنين مغنطيسي .كان الهدف من وراء هذه الدراسة معرفة النماذج السريرية ونماذج تخطيط الدماغ والرنين المغناطيسي لهؤلاء المرضى .وكانت النتيجة كالاتى : يتراوح معظم أعمار المرضى من عمر(15-30) سنة ومعظمهم حدثت لهم النوبات لأول مرة في فترة الطفولة الذكور والإناث يعانون من هذا المرض مع وجود ارتفاع في نسبة الذكور.معظم المرضى يعانون من حس شخصي يسبق النوبة الاشتدادية4/3المرضى لديهم نوبات جزئية معقدة .3/1 المرضى لديهم تشنجات ثانوية شمولية .التشنجات الحمية في فترة الطفولة والتهاب المخ و السحايا يمثلون عوامل خطورة فيما بعد. معظم الحالات لديها تغييرات غير طبيعية في تخطيط الدماغ . 4/1 الحالات فقط لديها تغييرات في الرنين المغنطيسي . ولذا ننصح بالفحص السريري الدقيق لكل حالات مرضى صرع الفص الصدغي طلب تخطيط دماغي ورنين مغناطيسي لكل الحالات وعلاج التشنجات المصاحبة للحمى فىالطفولة بعناية شديدة لتفادي حدوث مضاعفات فيما بعد.

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# Introduction and Literature Review

## 1. Epilepsy

### 1.1 Definition:

Epilepsy is a disorder characterized by the occurrence of at least 2 unprovoked seizures. Seizures are the manifestation of abnormal hyper synchronous discharges of cortical neurons. The clinical signs or symptoms of seizures depend upon the location and extent of the propagation of the discharging cortical neurons. That seizures are a common nonspecific manifestation of neurological injury and disease should not be surprising, because the main function of the brain is the transmission of electrical impulses[1]

### 1.2 .1 Classification of epileptic seizures [2]

In 1981, the International League Against Epilepsy (ILAE) developed an international classification of epileptic seizures that divides seizures into 2 major classes: partial-onset seizures and generalized-onset seizures. Partial-onset seizures begin in one focal area of the cerebral cortex, while generalized-onset seizures have an onset recorded simultaneously in both

cerebral hemispheres. Some seizures are difficult to fit into one particular class, and they are considered as unclassified seizures.

## 1. Partial-onset seizures

Partial-onset seizures are further classified into 3 categories:

I.Simple partial seizures.

II. Complex partial seizures.

III. Secondarily generalized tonic-clonic seizures.

Simple partial seizures: The key defining element of simple partial seizures is the occurrence of a seizure with preservation of consciousness. Many patients with complex partial seizures have an aura warning them of their seizure. An aura is a simple partial seizure. Many kinds of simple partial seizures exist, including sensory, motor, autonomic, and psychic experiences. Essentially, any discrete human experience that involves the cerebral cortex could be a simple partial seizure. The diagnosis is based upon the repeated stereotypic occurrence of the same experience in association with focal electroencephalography (EEG) changes, or the diagnosis is made after a recurrent aura occurs leading to a complex partial seizure or a secondarily generalized seizure. The disappearance of the

recurrent clinical phenomena with the use of anticonvulsants is presumptive but not diagnostic evidence for epileptic seizures.

The clinical diagnosis is quite difficult, as many stereotypic auras may be induced in areas of the cerebral cortex that are not recorded well by a typical EEG. Only 20-40% of auras have an ictal correlate in the scalp EEG. Simple partial seizures may last a few seconds to a few minutes. However, if the aura lasts longer than 30 minutes, it is considered simple partial status epilepticus.

Complex partial seizures: Consciousness is impaired during a complex partial seizure. In practice, assessing historically whether consciousness was impaired is difficult. The most common way to assess preservation of consciousness is by asking patients whether they were able to recollect the event. In many occasions, patients are able to remember their aura but are unaware that they were briefly unable to respond to the environment. Typically, a complex partial seizure begins with behavioral arrest and is followed by staring, automatisms, and postictal confusion. Frequently, the automatisms consist of chewing, lip smacking, mumbling, and fumbling with the hands. Dystonic posturing of the contra-lateral upper extremity often is seen when a complex partial seizure originates from the mesial

temporal lobe. A typical complex partial seizure lasts about 60-90 seconds and is followed by brief postictal confusion. However, generalized weakness, asthenia, and fatigue may last for a few days.

Complex partial seizures of frontal lobe origin may feature bizarre motor behaviors such as bicycling or a fencing posture. They have more prominent motor features than complex partial seizures of temporal lobe onset. The great majority of complex partial seizures have an ictal correlate in the EEG. The presence of normal alpha rhythm during the period of behavioral impairment of consciousness raises the suspicion for nonepileptic seizures.

Secondarily generalized seizures: These seizures often begin with an aura that evolves into a complex partial seizure and then into a generalized tonic-clonic seizure. However, a complex partial seizure may evolve into a generalized tonic-clonic seizure, or an aura may evolve into a generalized tonic-clonic seizure without an obvious complex partial seizure. Clinically, classifying a generalized tonic-clonic seizure by history alone as being secondarily generalized (partial onset) or primarily generalized is difficult. In most cases, the more severe a secondarily generalized seizure, the more it is associated with prominent amnesia for the aura.

## 2. Generalized-onset seizures

Generalized-onset seizures are classified into 6 major categories:

I.absence seizures.

II. Tonic seizures.

III. clonic seizures.

IV. myoclonic seizures.

V. Primary generalized tonic-clonic seizures.

VI. atonic seizures.

Absence seizures: These are brief episodes of impairment of consciousness with no aura or postictal confusion. They typically last less than 20 seconds and are accompanied by few or no automatisms. Facial automatisms are most frequent, and repetitive blinking is the most common facial automatism. Absence seizures often are precipitated by hyperventilation or photic stimulation. They typically begin during childhood or adolescence but may persist into adulthood. A diagnosis of new-onset absence seizures in adulthood is incorrect in the vast majority of cases. Often, those adult patients have complex partial seizures with

relatively minor automatisms. In children, absence seizures often are unrecognized until a child develops a generalized tonic-clonic seizure and are brought to medical attention. A sudden decreased performance in school grades or overall attention is a subtle manifestation of frequent absence seizures.

The classic ictal EEG correlate of absence seizures consists of 3-5Hz generalized spike and slow wave complexes. A significant inherited predisposition for typical childhood absence seizures exists, as demonstrated by twin studies. The EEG abnormality may persist into adulthood despite the absence of further clinical seizures. However, the electroencephalographic discharges in adults occur less often, are less well formed, and are of lesser amplitude than those recorded in affected children.

Myoclonic seizures: This seizure type consists of brief, arrhythmic, jerking, motor movements that last less than a second. Myoclonic seizures often cluster within a few minutes. If they evolve into rhythmic jerking movements, they are classified as evolving into a clonic seizure. Myoclonus is not always epileptic in origin. For example, the myoclonic jerks during phase I of sleep are normal “release” phenomena. The classic ictal correlate

of myoclonic seizures in the EEG consists of fast polyspike and slow wave complexes.

Clonic seizures: This seizure type consists of rhythmic, motor, jerking movements with impairment of consciousness. Clonic seizures also could have a focal origin with or without impairment of consciousness. The focal seizures are classified as simple or complex partial seizures. Typically, generalized clonic seizures simultaneously involve the upper and lower extremities. The ictal EEG correlate consists of bilateral rhythmic epileptiform discharges.

Tonic seizures: This seizure type consists of sudden-onset tonic extension or flexion of the head, trunk, and/or extremities for several seconds. Typically, these seizures occur in relation to drowsiness, shortly after falling asleep, or just after awakening. They often are associated with other neurologic abnormalities. The ictal correlate of tonic seizures in the EEG includes an electrodecremental response, which is a high-frequency electrographic discharge in the beta frequency (also known as "beta buzz") with a relatively low amplitude compared to the background rhythm and may evolve into slow spike-and-wave complexes or diffuse polyspikes.

Tonic-clonic seizures: This seizure type commonly is referred to as "grand mal" seizures. They consist of several motor behaviors including generalized tonic extension of the extremities lasting for few seconds followed by clonic rhythmic movements and prolonged postictal confusion. Clinically, the only behavioral difference between these seizures and secondarily generalized tonic-clonic seizures is that these seizures lack an aura. However, the aura preceding the secondarily generalized seizure often is forgotten because of postictal amnesia. The ictal correlate of generalized tonic-clonic seizures consists of generalized (bilateral) spike or polyspike and slow wave complexes. Often these epileptiform discharges have higher amplitude in the frontal regions.

Atonic seizures: This seizure type occurs in people with significant neurological abnormalities. These seizures consist of brief loss of postural tone, often resulting in falls and injuries. The ictal EEG correlate is similar to abnormalities observed in tonic seizures.

## 3. Unclassified seizures

Each seizure type is classified by its clinical and EEG manifestations. Occasionally, classifying seizures is difficult despite videotape review of the data.

## 1.2.2: Classification of epileptic syndromes

Epileptic seizures are symptoms of neurological dysfunction and are but one manifestation of many neurological diseases. Like any other syndrome in medicine, an epileptic syndrome is a group of signs and symptoms that share a common pathogenesis, prognosis, and response to treatment[2]

## Revision of International classification of epilepsies and epileptic syndromes

In 1989, the ILAE developed a classification of epileptic syndromes. At the present time, a task force is revising this syndromatic classification. The current system comprises 2 major categories: localization-related syndromes and generalized-onset syndromes. Ideally, physicians would classify the seizures of their patients using the classification for seizure types, and if possible, make a syndromatic diagnosis.

 Localization-related epilepsies and syndromes

- Idiopathic with age-related onset
- Benign childhood epilepsy with Centro-temporal spikes
- Childhood epilepsy with occipital paroxysms

- Symptomatic

 Generalized epilepsies and syndromes

- Idiopathic with age-related onset
- Benign neonatal familial convulsions
- Benign neonatal convulsions
- Benign myoclonic epilepsy of infancy
- Childhood absence epilepsy (pyknolepsy)
- Juvenile absence epilepsy
- Juvenile myoclonic epilepsy
- Epilepsy with grand mal seizures on awakening
- Idiopathic and/or symptomatic infantile spasms
- Lennox-Gastaut syndrome
- Epilepsy with myoclonic astatic seizures
- Epilepsy with myoclonic absences
- Symptomatic

The International Classification has been shown to be reasonably useful in the clinical setting, but its limitations have prompted recent calls for a revision and a classification based exclusively on ictal semiology (detailed clinical description of the child's behavior during a seizure), as opposed to the current classification, which is actually a classification of electro-clinical syndromes[3]. The International League against Epilepsy has appointed four committees to prepare documents on terminology for ictal phenomenon, classification of epileptic seizures based upon known or presumed path-physiological and anatomic substrates, a classification of epileptic syndromes and epileptic diseases, and a new classification of functional disability caused by seizures or epilepsy[4]

## 1.3 Historical background

Epileptic seizures have been recognized for several millennia. One of the earliest descriptions of a secondarily generalized tonic-clonic seizure was recorded over 3000 years ago in Mesopotamia. The seizure was attributed to the god of the moon. Epileptic seizures were described in several ancient cultures, including China, Egypt, and India. An ancient Egyptian papyrus described a seizure in a man who had experienced prior head trauma. Hippocrates wrote the first book about epilepsy almost 2500 years ago. He

rejected ideas regarding the divine etiology of epilepsy and concluded that it was caused by an excess of phlegm that caused abnormal brain consistency. Hippocratic teachings were forgotten, and divine etiologies again dominated beliefs about epileptic seizures during medieval times. Even at the turn of the last century, excessive masturbation was considered a cause of epilepsy. This hypothesis is credited as leading to the use of the first effective anticonvulsants, bromides.

The modern era on the investigation of the etiology of epilepsy began with the work of Fritsch, Hitzig, Ferrier, and Caton in the 1870s. They recorded and evoked epileptic seizures in the cerebral cortex of animals. In 1929, Berger discovered that electrical brain signals could be recorded from the human head with scalp electrodes; this discovery led to the use of EEG to study and classify epileptic seizures. Gibbs, Lennox, Penfield, and Jasper further advanced the understanding of epilepsy and developed the system of the 2 major classes of epileptic seizures currently in use. An excellent historical review of seizures and epilepsy, written by E. Goldensohn, commemorating the 50th anniversary of the creation of the American Epilepsy Society[5] .

## 1.4 Epidemiology:

The age-adjusted prevalence of epilepsy in developed countries is 4 to 8 per 1,000 population[6] An estimated 1 percent of children and adolescents in the United States will experience at least one a febrile seizure by age 14; prevalence studies for active epilepsy (occurrence of a seizure within the previous five years or control of seizures by medication) report 4 to 9 cases per 1,000 children. In one study of 10-year-old children, the lifetime prevalence of childhood epilepsy was 6 per 1,000[7] . Of all children, 3 to 5 percent will have a single febrile seizure in the first five years of life; 30 percent will have additional febrile seizures, and 3 to 6 percent of those with febrile seizures will develop a febrile seizures or epilepsy. There is a 3.6 percent risk of experiencing at least one seizure in an 80-year lifespan[7].

The onset of epilepsy most commonly is at the extremes of life[8].The incidence in developed countries is highest in the first few months of life, particularly in the immediate postnatal period, falls significantly after the first year of life, is stable during the first decade, and then falls again in adolescence. Incidence is lowest in young and middle adulthood and begins increasing in the 50s, with a dramatic increase after age 60 when

the incidence exceeds that of infancy. The incidence profile is quite different in developing countries, where the peak in the elderly usually is absent and the highest incidence occurs in young adults[9].

## 1.5 Etiology:

Seizures can arise from any site in the brain but typically are localized to the neocortical gray matter and the limbic system, particularly the hippocampus and amygdala. The thalami, basal ganglia, and posterior fossa structures, including the cerebellum, generally are considered incapable of generating seizures but participate as neuromodulatory influences or relay stations for the spread of a seizure from a cortical or limbic origin. One case report, however, questioned this long-standing dogma by describing electrographic seizures (recordings from surgically implanted depth electrodes) and clinical seizures arising in the cerebellum of a six-month-old infant with a posterior fossa ganglioglioma[10].

An epidemiologic study in Rochester, Minnesota reported that the largest percentage of individuals with epilepsy fall into the idiopathic/cryptogenic category, followed in order by vascular, traumatic, developmental (conditions manifested by mental retardation and/or cerebral

palsy presumed to be present from birth), infectious, neoplastic, and degenerative causes[6].

Neurodevelopmental lesions (NDL): The MRI has markedly increased our ability to recognize neurodevelopmental lesions that were unrecognized in life; future classification schemes will have to include sections for these lesions. Many of them are not seen with routine CT scans, which are entirely normal or may show areas of nonspecific atrophy or signal abnormality. The terminology is confusing; NDL also is referred to as "cortical dysplasia," "cortical dysgenesis," "malformations," and "disorders or malformations of cortical development"[11].

Developmental lesions result from a disruption of one or more of the three major steps in the normal development of the cerebral cortex[12].

These disorders have been classified according to MRI findings into focal, hemispheric, or generalized/multifocal. The generalized NDL include, pachygyria, and band, laminar, and subependymal heterotopia. The most common hemispheric NDLs are Sturge-Weber syndrome (associated with facial angiomatous nevi) and hemimegalencephalophy (enlargement of an entire hemisphere from diffuse migrational and dysplastic changes). More limited NDLs include focal cortical dysplasia, schizencephaly (cleft

extending from the ventricle to the cortical surface usually lined with dysplastic cortex), polymicrogyria, and subependymal heterotopias. One group has provided a classification based upon the embryological, anatomical, and genetic bases of the developmental disorders[13]. They divided the malformations into four broad categories:

• Malformations caused by abnormal neuronal and glial proliferation

• Malformations caused by abnormal neuronal migration

• Malformations caused by abnormal cortical organization

• Developmental cortical malformations, not otherwise specified.

The clinical and radiographic findings of 109 children with malformations of cortical development were reported from a radiological database in a major pediatric hospital[14]. Seizures were present in 75 percent, developmental delay or intellectual disability in 68 percent, abnormal neurological findings in 48 percent, and congenital anomalies apart from the CNS malformations in 18 percent. The main NDLs found were heterotopic gray matter (19 percent, clumps of neurons in the white matter or near the ventricular wall which failed to migrate to the cerebral mantle), cortical tubers (17 percent, associated with tuberous sclerosis),

focal cortical dysplasia (16 percent), polymicrogyria (16 percent, small, malformed cortical gyri), agyria (absent or simple sulcation)/pachygyria (15 percent, thickened cortex with broad gyri), schizencephaly/cleft (5 percent), transmantle dysplasia (5 percent, malformation extending from the wall of the lateral ventricle outward to the cortical surface) and hemimegalencephalopathy (4 percent). Many of the NDLs are associated with recognizable somatic malformations and some with well-defined chromosomal defects[15].

**Socioeconomic status as a risk factor for the development of epilepsy:**

Epilepsy is associated with a wide range of markers of social and economic disadvantage, including poor academic achievement, unemployment, underemployment, and low income.[16-19] Because of this association it is often assumed that people who are socially and economically deprived are more likely to develop epilepsy. This hypothesis is supported to some extent by the observation that the incidence of epilepsy is higher in developing countries than in developed countries.[20]

## 1.6 Investigations:

### 1.6.1 Electroencephalogram:

EEG is particularly useful in the analysis of seizure disorders. Paroxysmal abnormalities are common between overt seizures (interictally) as well as during seizures (ictally). Such abnormalities include spike and sharp waves:

• A spike is a single wave that stands out from background activity and has duration of less than 80 milliseconds.

• A sharp wave is similar to a spike but has duration of more than 80 milliseconds.

A spike or sharp wave is often followed by a slow wave, and spikes and slow waves can alternate at frequencies from 2 to 5 Hz. Epileptic paroxysmal abnormalities can be generalized or focal. The classic generalized abnormality is the 3 Hz spike and wave pattern which underlies the petit mal absence attack in children .A typical focal abnormality is a focal single spike followed by a slow wave .This abnormality can be seen in focal epilepsy or secondary generalized epilepsies occasionally, the abnormal activity spreads to the other hemisphere. If the abnormal

electrical activity spreads rapidly to the entire brain, the EEG will be indistinguishable from that of a generalized seizure[21].

### 1.6.2 Neuroimaging:

The majority of epilepsies with structural abnormalities visible on computed tomography scan (CT) or magnetic resonance imagings (MRI) are caused by neoplasms, malformative processes, neurocutaneous syndromes, and the static encephalopathies following trauma, infections, and hypoxic-ischemic insults. A CT scan is a satisfactory screening test for some of these conditions, particularly larger neoplasms, old infarctions, and major malformative processes, and is ideal for emergency room assessment of the critically ill patient or one who cannot tolerate anesthesia. It will also identify better than will MRI calcifications in congenital infections and some of the neurocutaneous syndromes (e.g. tuberous sclerosis). The most economic approach in evaluating a patient with seizures, however, is to perform MRI, which provides a much more detailed assessment of brain anatomy and is a better screen for central nervous system (CNS) malformations and dysplastic lesions. It is also the best imaging technique for looking at subtle temporal lobe pathology, particularly in the hippocampus, a common site of seizure onset. Special thin cuts with

nonstandard imaging angles are necessary to adequately assess hippocampal anatomy[22].

### 1.6.3 Laboratory screening:

A search should be made for an underlying metabolic, genetic or neurodegenerative disorder if no specific structural lesion is found (e.g. tumor or CNS malformation) and the etiology of the seizures is not apparent on the history and physical examination. In infants and children with unexplained seizures, particularly those with static encephalopathies including developmental delay, mental retardation, and abnormal neurological examinations, serum (and often CSF) amino acid analysis, urine for quantitative organic acids, serum calcium, glucose, carnitine, ammonia, lactate and pyruvate, routine chromosomal karyotype (virtually all chromosomal syndromes can manifest seizures), and DNA analysis for fragile X syndrome, particularly in boys and occasionally in girls with maternal family histories of mental retardation. With regard to the last study, it is well known that approximately 20 percent of males with fragile X syndrome have seizures, but physicians are less aware that female carriers of fragile X syndrome, even some with normal intelligence, can

have seizures and focal EEG abnormalities identical to those seen in males and resembling benign rolandic epilepsy[23].

### 1.7 Chronic Epilepsy:

Aprogressive cerebral damage resulting from the cumulative effect of epileptic seizures has been a source of great preoccupation among patients and clinicians alike. Prospective data on this issue, however, are sparse and remain the source of controversy.

Intractable epilepsy may be associated with widespread structural cerebral damage. Significant quantitative changes in individuals were largely attributable to preexisting cerebral lesions or alcohol abuse .Cerebral damage may occur before the onset of seizures or develop insidiously over a more prolonged period.[24]

## 1.8 FIRST SEIZURE

### 1.8.1 Incidence:

A first "grand mal" convulsion is frightening, yet prospective, population-based studies indicate that we all face an 8-10% lifetime risk of one seizure[25] and a 3% chance of epilepsy.[26] It seems likely that everyone could have a seizure if a particular set of circumstances occur—but some people have a lower seizure threshold than others. A first seizure caused by

an acute disturbance of brain function (acute symptomatic or provoked) is unlikely to recur (3-10%). If a first seizure is unprovoked, however, meta-analyses suggest that 30-50% will recur; and after a second unprovoked seizure, 70-80% will recur, justifying the diagnosis of epilepsy (a tendency for recurrent seizures).[27-29]

**1.8.2 Differential diagnosis**:

The differential diagnosis for a first seizure is wide. Most important in our experience are syncope (including breath holding and pallid syncope), transient ischaemic attacks, metabolic encephalopathy (including hypoglycaemia or electrolyte disturbance), sleep walking, night terrors, complex migraines, cardiac arrhythmias, and pseudoseizures. "Convulsive syncope" presents a particular challenge when syncope provokes a post-anoxic convulsion. A detailed history from both patient and witness is paramount, but no single feature is diagnostic. Tongue biting is not common but is fairly specific for a convulsive seizure, while postictal confusion suggests a seizure. If the first event is ambiguous, we advocate waiting for a recurrence for clarification. In our experience, and as outlined in a thoughtful review, misdiagnosis of an "epileptic" seizure may be more stigmatising than a delayed diagnosis of epilepsy.[30]

Once an acute provoking cause has been excluded, the next step is to decide if the first seizure indicated a focal or generalised epilepsy syndrome—a critical distinction if drug treatment is considered. An epilepsy syndrome can be diagnosed after one seizure, even though a single seizure is insufficient for the diagnosis of epilepsy.[31] The diagnosis of epilepsy addresses recurrence risk, whereas epilepsy syndrome is a broader concept encompassing age of onset, aetiology, prognosis, and response to treatment. For example, a child with a first nocturnal seizure and typical EEG spikes can be diagnosed as having benign rolandic epilepsy, a disorder of genetic aetiology that constitutes 15% of childhood epilepsy and nearly always remits.

Population based studies indicate that 25-30% of first seizures are "acute symptomatic" or "provoked" by a brain insult or a metabolic or toxic disturbance of brain function.[32-34]

### 1.8.3 Investigations:

A practice parameter noted little justification for routine investigations of blood, urine, and cerebrospinal fluid in children; however, the circumstances of a first seizure should direct investigations.[35]

If a first seizure is unprovoked, large case series support the value of electroencephalography (EEG), and often magnetic resonance imaging (MRI), to identify the cause.[35,36] Such images cannot be used to diagnose the event—the diagnosis can only be made from the patient's history. The value of EEG is to point to focal lesions (especially localised slow waves), predict recurrence, and indicate a specific epilepsy syndrome (spike pattern). When performed within 24-48 hours of a first seizure EEG shows substantial abnormalities in about 70% of cases.[31,37] The yield may be lower with longer delays after the seizure. When standard EEG is negative, systematic case series have shown that sleep deprived EEG will detect epileptiform (spike) discharges in an additional 13-31% of cases.[31,37]

Several case series comparing MRI with computed tomography in the same patient indicate that the latter may not detect small tumours or other subtle pathologies [31] After a first seizure, abnormalities detected by MRI that lead directly to intervention are more common in adults than children.[38] In a series of 166 adults with a first seizure, the most common aetiologies diagnosed with both computed tomography and MRI were cerebrovascular lesions (26%), brain tumours (12%), traumatic scar formations (5%), and other conditions (4%).[39] Subcortical vascular encephalopathy itself is also

associated with an increased risk for seizures.[40] In elderly people, a first seizure may be caused by a silent stroke only recognizable by MRI.

### 1.8.4Prognosis:

A meta-analysis concluded that the risk of recurrence after a first unprovoked seizure was 42% over the next two years.[41] The significance of two definite unprovoked seizures within 24 hours is uncertain. One prospective study suggested that these two attacks should be viewed as a single, first seizure,[29] whereas another concluded they should be viewed as separate events, permitting a diagnosis of epilepsy.[42]

Meta-analysis of case series[41] shows that about 60-70% of recurrences are within six months of the first seizure, with an exponential decrease in risk thereafter. The strongest risk factors for recurrence are aetiology (pre-existing brain abnormalities indicate "remote symptomatic" epilepsy) and EEG abnormalities, especially focal spikes.[27,37,41]

Restrictions to recreational activity after a first untreated, unprovoked seizure should be individualised and limited to two or three months for children and adults.[43]

Among neurologists there is a growing consensus that non-commercial drivers with a first unprovoked seizure should stop driving only for three to six months, especially those with favourable prognostic factors. If a first seizure was acute symptomatic, then most patients should be able to drive within three months. Commercial drivers with an unprovoked seizure should be subject to a more restrictive rule (such as at least two years seizure-free without medication).[44]

Drug treatment after a first seizure is controversial.[45-48] A practice parameter about first seizures in children concluded that antiepileptic drugs decrease but do not eliminate seizure recurrence and have no effect on long term remission.[47] Two large recent randomised studies of children and adults compared antiepileptic drugs with no treatment after a first seizure and came to an identical conclusion.[46,47] Any decision to start treatment must weigh the risk of another seizure against the risks of side effects from chronic drug treatment.[45-47]

There are no published data to guide length of treatment after a first seizure in adults. Each case must be viewed individually, including consideration of the medical and social consequences of another seizure. It is tempting to use EEG and neuroimaging to help with this decision because persistent EEG abnormalities, and a documented aetiology, are associated

with a higher risk of relapse when antiepileptic drugs are withdrawn after several years of remission (affirmed by a meta-analysis).[49]

## 1.9Epilepsy in Elderly

### 1.9.1Epidemiology:

Systemic disorders precipitating acute seizures can involve metabolic or electrolyte disturbances, including hypoglycaemia and hyperglycaemia, uraemia, hyponatraemia, hypocalcaemia, hypothyroidism, pneumonia, urosepsis, and hepatic failure.[50] Seizures secondary to acute central nervous system infections occur more commonly in developing countries than in developed countries.

The annual incidence of epilepsy (recurrent unprovoked seizures) rises from 90 per 100 000 in people between the ages of 65 and 69 to more than 150 per 100 000 for those over 80.[51]

In developed countries, the most common cause of provoked seizures in elderly people is acute stroke.[52] Eight per cent of patients will develop seizures within two weeks of a haemorrhagic stroke, compared with 5% among those who have had an ischaemic event.

A wide range of drugs commonly taken by elderly people have been reported to precipitate seizures, including antipsychotics, antidepressants, antibiotics, theophylline, levodopa, thiazide diuretics.[53]

Older people who present with a first unprovoked seizure are more likely to develop seizure recurrence than are younger adults.[54] Epilepsy is usually diagnosed after the occurrence of two or more unprovoked seizures. A cause can be identified in more than 60% of elderly people with epilepsy; this is classified as "remote symptomatic epilepsy."[55] Previous stroke is the most common underlying problem, accounting for 30-40% of all cases of epilepsy. Asymptomatic cerebral infarction can also lead to epilepsy, and, paradoxically, seizures may be a marker of increased risk for subsequent stroke.[56]

Alzheimer's disease and other dementias are associated with a fivefold to 10-fold increase in the risk of epilepsy, which usually develops in the advanced stage.[57] Brain tumours and head trauma are relatively uncommon causes of epilepsy in elderly people.[55]

### 1.9.2Presentation:

Compared with younger patients, the presentation of epilepsy in old age

is often less specific, and it may take time before a firm diagnosis can be reached. Under diagnosis and misdiagnosis are common.

### 1.9.3Diagnosis:

Routine scalp electroencephalography is not sensitive or specific for the diagnosis in elderly people, nor does the absence of epileptiform abnormalities rule out epilepsy.[58]

### 1.9.4Treatment:

Treatment for provoked seizures should be directed towards the underlying cause. All elderly people reporting more than one well documented or witnessed unprovoked event should be offered antiepileptic drug treatment. Whether treatment should be started after a single unprovoked seizure remains controversial. Prospective randomised studies involving patients across all age groups, such as the recently published multicentre study of early epilepsy and single seizures (MESS**)** study,[59] have shown that, compared with deferring treatment until further episodes have occurred, immediate treatment after a first unprovoked seizure does not improve the long term remission rate. However, because of the physical and psychological consequences of recurrence, prophylactic treatment should be considered after a first unprovoked event in an elderly person at high risk of

recurrence, such as those with a causative brain lesion or an epileptiform electroencephalogram, or at his or her request.

Epilepsy in elderly people generally responds well to treatment. Up to 80% of patients with onset in old age can be expected to remain seizure-free with anti-epileptic drug treatment. [60] Elderly people are, however, more susceptible to the adverse effects of drugs than their younger counterparts.[61] Whether treatment can be safely withdrawn after a period of seizure freedom has not been determined, so most older patients will remain on antiepileptic drugs for life. Age related alteration in receptor affinity and number may lead to altered drug sensitivity and impaired homoeostasis.[62] Few data specific to elderly people are available to help the clinician to choose the best treatment for the individual patient.[50] All the established antiepileptic drugs, with the exception of ethosuximide, are efficacious against partial seizures with or without secondary generalisation, the typical seizure type in elderly people.[63] Carbamazepine may have a small benefit over sodium valproate for control of partial seizures,[64] but no trial has specially included elderly patients. The barbiturates are not generally recommended for use in elderly people because of their sedative and behavioural side effects.[65]

Phenobarbital, phenytoin, and carbamazepine can produce idiosyncratic reactions, in particular skin rashes, and complex drug-drug interactions, as they are all substrates for and inducers of hepatic monooxygenase enzymes. They can interact with a wide range of lipid soluble drugs commonly used in elderly people, including warfarin, cardiac antiarrhythmics, theophylline, corticosteroids, antidepressants, cytotoxics, macrolide antibiotics, and St John's wort.[66]

Enzyme induction also accelerates the catabolism of vitamin D, leading to decreased calcium absorption, secondary hyperparathyroidism, and increased bone loss.[67] Sodium valproate has a broad spectrum of activity and is the drug of choice for the unusual idiopathic generalised epilepsy syndrome presenting late in life. It may have a slightly better cognitive and behavioural profile than the other established antiepileptic drugs.[65]

None of the modern antiepileptic drugs has been shown to have superior efficacy to the established agents for the treatment of newly diagnosed partial and tonic-clonic seizures,[63] although lamotrigine and oxcarbazepine have shown better tolerability,[68,69] increasing the likelihood of a successful outcome. Only two randomised controlled trials have specifically recruited elderly patients; these found that lamotrigine and gabapentin produced fewer adverse events than carbamazepine, with similar

efficacy.[70] [71] Pooled data from 13 trials of lamotrigine involving elderly patients have confirmed its good tolerability profile.[72] Open label studies have indicated that levetiracetam may be effective in this population.[73]

### 1.9.5 Psychosocial implications:

Epilepsy can have a profound physical and psychological impact in old age. Elderly people are particularly vulnerable to injuries during seizures. The clinical situation is often complicated by a range of neurodegenerative, cerebrovascular, neoplastic, and psychiatric co- morbidities. Problems with concomitant drugs are common. The stigma associated with diagnosis of epilepsy can be particularly hard to deal with at this time of life.[74]

## 2. Temporal Lobe Epilepsy

### 2.1 Definition :

Temporal lobe epilepsy (TLE) was defined in 1985 by the International League against Epilepsy (ILAE) as a condition characterized by recurrent unprovoked seizures originating from the medial or lateral temporal lobe. The seizures associated with TLE consist of simple partial seizures without loss of awareness (with or without aura) and complex partial seizures (i.e.

with loss of awareness). The individual loses awareness during a complex partial seizure because the seizure spreads to involve both temporal lobes, which causes impairment of memory[75].

TLE was first recognized in 1881 by John Hughlings Jackson, who described "uncinate fits" and the “dreamy state." In the 1940s, Gibbs et al introduced the term "psychomotor epilepsy." [76]

The international classification of epileptic seizures (1981) replaced the term psychomotor seizures with complex partial seizures. The ILAE classification of the epilepsies uses the term temporal lobe epilepsy and divides the etiologies into cryptogenic (presumed unidentified etiology), idiopathic (genetic), and symptomatic (cause known, e.g. tumor).

## 2.2 Pathophysiology :

Hippocampal sclerosis is the most common pathologic finding in TLE. Hippocampal sclerosis involves hippocampal cell loss in the CA1 and CA3 regions and the dentate hilus. The CA2 region is relatively spared.[77]

## 2.3 History:

### 2.3.1 Aura:

In temporal lobe epilepsy (TLE), there is evidence of ictal and interictal autonomic dysregulation, predominantly with sympathetic overactivity. The effects of TLE surgery on autonomic cardiovascular control and on baroreflex sensitivity (BRS) have been studied After TLE surgery; there is a reduction of sympathetic cardiovascular modulation and BRS that might result from decreased influences of interictal epileptogenic discharges on brain areas involved in cardiovascular autonomic control. TLE surgery seems to stabilize the cardiovascular control in epilepsy patients by reducing the risk of sympathetically mediated tachyarrhythmias and excessive bradycardiac counter regulation, both of which might be relevant for the pathophysiology of sudden unexpected death in epilepsy patients (SUDEP). Thus TLE surgery might contribute to reducing the risk of SUDEP.[78]

Auras are a common feature of simple partial seizures and usually precede complex partial seizures of temporal lobe origin. Auras may be classified by symptom type; the types comprise somatosensory, special sensory, autonomic, or psychic symptoms.

. Somatosensory and special sensory phenomena:

Olfactory and gustatory illusions and hallucinations may occur. Auditory hallucinations consist of a buzzing sound, a voice or voices, or muffling of ambient sounds. This type of aura is more common with neocortical TLE than with other types of TLE[79].

Patients may report distortions of shape, size, and distance of objects.

These visual illusions are unlike the visual hallucinations associated with occipital lobe seizure in that no formed elementary visual image is noted, such as the visual image of a face that may be seen with seizures arising from the fusiform or the inferior temporal gyrus. Things may appear shrunken (micropsia) or larger (macropsia) than usual. Tilting of structures has been reported. Vertigo has been described with seizures in the posterior superior temporal gyrus.

. Psychic phenomena: Patients may have a feeling of déjà vu or jamais vu, a sense of familiarity or unfamiliarity, respectively. Patients may experience depersonalization (i.e. feeling of detachment from oneself) or derealization (i.e. surroundings appear unreal). Fear or anxiety usually is associated with seizures arising from the amygdala. Patients may describe a sense of dissociation or autoscopy, in which they report seeing their own body from outside.

. Autonomic phenomena are characterized by changes in heart rate, piloerection, and sweating. Patients may experience an epigastric "rising" sensation or nausea.

### 2.3.2 Physical:

. Following the aura, a temporal lobe complex partial seizure begins with a wide-eyed, motionless stare, dilated pupils, and behavioral arrest. Oral alimentary automatisms such as lip smacking, chewing, and swallowing may be noted. Manual automatisms or unilateral dystonic posturing of a limb also may be observed[80].

. Patients may continue their ongoing motor activity or react to their surroundings in a semipurposeful manner (i.e. reactive automatisms). They can have repetitive stereotyped manual automatisms.

 A complex partial seizure may evolve to a secondarily generalized tonic-clonic seizure.

 Patients usually experience a postictal period of confusion, which distinguishes TLE from absence seizures, which are not associated with postictal confusion. In addition, absence seizures are not associated with

complex automatisms. Postictal aphasia suggests onset in the language-dominant temporal lobe.

- Most auras and automatisms last a very short period—seconds or 1-2 minutes. The postictal phase may last for a longer period (several minutes). By definition, amnesia occurs during a complex partial seizure because of bilateral hemispheric involvement[81].

Panic disorder and some partial seizures may have similar symptoms. Panic disorder has a lifetime prevalence of about 1.5% and is characterised by discrete episodes of unexpected, sudden, overwhelming terror accompanied by a variety of physical, cognitive, and behavioural symptoms.[82]

Patients with epilepsy may have prodromal symptoms of tension, anxiety, and depression. Temporal lobe seizures commonly include affective symptoms, fear, and autonomic features, including changes in skin colour, blood pressure, and heart rate.[83] In comparison, for panic attack to be diagnosed patients must have at least four of 13 symptoms, including physical symptoms (palpitations, sweating, trembling, sensation of breathlessness, chest pain, feeling of choking, nausea, faintness, chills or flushes, and paraesthesiae) and affective symptoms, including fear of losing

control, fear of dying, and derealisation or depersonalisation. [82,84]There is, therefore, considerable overlap of symptoms between the two disorders, and a definitive diagnosis may be difficult. Differentiating partial seizures from panic disorder can be difficult on the basis of symptoms but is clearly important.[85-87]

The duration of the attack may be helpful; partial seizures tend to be much shorter than panic attacks, which can last between 5 and 30 minutes [88]

and routine electroencephalography may give normal results in patients with partial seizures (up to four wake and sleep recordings on electroencephalography may be needed to identify interictal epileptiform discharges in 90% or more of patients with confirmed epilepsy).[89]

The value of prolonged electroencephalography is in the differentiation of epileptic from non-epileptic attacks and the classification of seizure type.[90]

**2.4 Causes:**

.. The etiologies of TLE include the following:

o Past infections, e.g. herpes encephalitis or bacterial meningitis.

- Trauma producing contusion or hemorrhage that results in encephalomalacia or cortical scarring.
- Hamartomas.
- Gliomas.
- Vascular malformations (i.e. arteriovenous malformation, cavernous angioma).
- Cryptogenic: A cause is presumed but has not been identified.
- Idiopathic (genetic): This is rare. Familial TLE was described by Berkovic and colleagues, and partial epilepsy with auditory features was described by Scheffer and colleagues[91].

**2.5 Hippocampal Sclerosis:**

. Hippocampal sclerosis produces a clinical syndrome called mesial temporal lobe epilepsy (MTLE). MTLE begins in late childhood, then remits, but reappears in adolescence or early adulthood in a refractory form[92].

The introduction of MRI permitted identification of hippocampal atrophy and signal-intensity change in patients with TLE who were being

considered for epilepsy surgery.[93,94]The anatomic structure of the hippocampal formation in the temporal horn of the lateral ventricle facilitated detection of volume loss associated with hippocampal sclerosis.[94,95]The MRI-identified hippocampal structural changes were shown to be a surrogate for focal cell loss and proved to be a reliable indicator of the temporal lobe of seizure origin.[95]Hippocampal morphologic changes associated with hippocampal sclerosis have correlated with a favorable operative outcome in patients with medial TLE undergoing surgical treatment. Visual inspection alone is usually sufficient to identify unilateral or asymmetric hippocampal formation atrophy. Quantitative volumetric studies permitted an objective assessment of unilateral or bilateral hippocampal atrophy associated with neuronal loss and were useful for research applications.[93-96]

Previous studies using morphometric measurements have provided additional compelling evidence that extrahippocampal volume loss may occur in patients with medial TLE.[94-99]The volume diminution occurred predominantly in gray matter structures directly connected to the epileptogenic hippocampal formation, such as the amygdala and entorhinal cortex, and may represent neuronal cell loss.[95,99]The maximal region of atrophy is usually ipsilateral to the epileptic temporal lobe.[94,95,99] Volumetric

abnormalities also have been identified in the basal ganglia and cerebellum.[96-98]The structural neuroimaging alterations have been most prominent in patients with hippocampal atrophy.[94,98]Long-term intracranial EEG recordings in one series demonstrated that the localization of the ictal-onset zone was concordant with the entorhinal cortical atrophy in 63% of patients with medial TLE.[99]

A potential mechanism for these structural changes includes the anatomic and functional connections to the hippocampus in patients with medial TLE.[94-100]The studies by Bonilha et al. and Gonçalves Pereira et al. support the hypothesis that direct connections between neuronal structures and the mesial temporal lobe account for the temporal lobe and thalamic structural alterations. Previous reports also suggested that the relation between the hippocampus and amygdala as well as between the entorhinal and perirhinal areas may explain the volume diminution ipsilateral to the epileptic temporal lobe. Another pathogenesis to be considered for the widespread morphologic alterations may be the recurrent seizures or the underlying symptomatic proconvulsant etiology.[101]Conflicting evidence concerns the effect of repetitive seizure activity on neuronal function and structure.[101]Recurrent seizures induce brain plasticity that may result in either neuronal cell loss or neuroprotection[101] .Intractable epilepsy or

generalized convulsive status epilepticus may induce progressive neuronal loss, hippocampal atrophy, and increase in susceptibility to network synchronization[98,101] .The presence of generalized tonic–clonic seizures in one study did not correlate with hippocampal formation atrophy[101] .Variably, sequential MRI studies in patients with intractable partial epilepsy show progressive hippocampal and extrahippocampal volume loss related to the repetitive seizures .[98,101]

Potentially, seizure propagation to gray matter structures and the subcortical white matter connected to the medial temporal lobe may be the basis for the more extensive morphologic alterations.[96-98]

Several pivotal questions remain to be answered regarding the implications and significance of these interesting neuroimaging observations. Ultimately, longitudinal studies using MRI will be necessary to see whether progressive morphologic abnormalities occur in patients with TLE[101].

**2.6 Febrile Seizures and Mesial Temporal Sclerosis**

Data from large cohorts of children with febrile seizures indicate that in 2% to 10% of children who have febrile seizures, unprovoked seizures or epilepsy will subsequently develop[102-109].

The types of epilepsy that occur in children with prior febrile seizures are varied and not very different than those that occur in children without such a history.[102,109,110] In Japanese children, an increased incidence of febrile seizures is not associated with an increased incidence of epilepsy[111]. Furthermore, in randomized clinical trials, drugs such as phenobarbital or diazepam, which reduced the risk of recurrent febrile seizures, do not alter the risk of subsequent epilepsy[112-114]. The weight of the epidemiologic data argues against a causal association in the majority of cases.

Febrile status epilepticus (SE), which is the extreme end of complex febrile seizures, accounts for approximately 5% of all febrile seizures [115]and for 25% of all pediatric SE [116].If febrile seizures cause MTS and TLE, then patients at highest risk should be those with febrile SE (duration 30 min). However, the data from prospective outcome studies of febrile SE, unfortunately, are inconclusive. Studies of febrile SE[102,104,115,117] all report a much higher risk of epilepsy, but they have not specifically addressed whether an increased risk of TLE occurs, and no imaging data are available on these cohorts, so that the incidence of MTS cannot be assessed.

Inherent limitations are found in the ability of epidemiologic studies to address the relation between prolonged febrile seizures and MTS or TLE. If

TLE is used as the outcome, the latency period between febrile seizures and the subsequent development of recognizable TLE is quite long, averaging 8 to 11 years [102,118,119] Recent data from the multicenter study of epilepsy surgery indicate that there may be an even longer latency period before epilepsy becomes intractable [120].The latency issue could be overcome by substituting anatomic MTS, which occurs more quickly, as the designated outcome; however, MTS has not yet been established as a valid surrogate for TLE.

Another serious limitation of epidemiologic studies in establishing a causal relation between febrile seizures and MTS or TLE is the relative rarity, at least in humans, of the target event (i.e., both febrile seizures and MTS and/or TLE). The various studies that examine the relation between prolonged febrile seizures and MTS report a mean duration of febrile seizure of 90 to 100 minutes in those patients with subsequent MTS[102,121-123] .Less than 1% of cases of febrile seizures are both focal and longer than 60 minutes[115,124]. As with prolonged seizures, acute injury and/or subsequent MTS do not occur in all cases. Therefore, the number of subjects needed to find an effect, with only epidemiologic techniques, is huge and well beyond the numbers seen in any of the published epidemiologic series thus far. Given the high frequency of prior febrile seizures in patients with epilepsy

for whom the febrile seizures clearly are a marker for increased seizure susceptibility, it is not surprising that epidemiologic studies have not detected the relatively small number of cases of MTS and TLE in which a causal relation between prolonged febrile seizures and MTS or TLE actually exists.

Magnetic resonance imaging (MRI) has demonstrated abnormalities in the hippocampus after prolonged febrile seizures [102,123,125] .The changes may be transient and, therefore, not detected, unless MRI is performed shortly after the prolonged seizure. MRI is requisite to the detection of chronic hippocampal injury, such as in MTS. Although hippocampal MRI abnormalities may be seen after prolonged febrile seizures, it is not clear how to predict whether the abnormality will be permanent. Nevertheless, the best available data for a causal relation between prolonged febrile seizures and MTS come from imaging studies.

The most interesting data to address the causal relation issue come from recent prospective studies of febrile SE that have imaged affected children within 72 hours of the seizure [123,125]. VanLandingham et al. [123] described 27 infants aged between 8 and 24 months who were imaged after prolonged febrile seizures. They reported acute hippocampal MRI abnormalities in four

of the 15 infants with focal or lateralized prolonged febrile seizures and in none of the 12 infants with generalized prolonged febrile seizures. The mean seizure duration in those showing acute changes was 99 minutes, compared with 41 minutes in those with focal seizures and 46 minutes in those with generalized febrile seizures who did not have acute imaging abnormalities. Notably, only those children whose seizures were both focal and prolonged had evidence of either acute changes or later MTS. It is difficult to distinguish which feature is most important, as the majority of very prolonged febrile seizures are focal[115] .However; at least two other studies on the association between prolonged febrile seizures and MTS reported that the mean duration of the febrile seizure in cases with MTS was 90 to 100 minutes.[121,122]

The group of investigators at Duke University has enlarged and further researched the original cohort of 27 children studied by VanLandingham et al.[125] On careful reexamination, 30% of MRIs done within 72 hours of the prolonged febrile seizures were abnormal on visual inspection by blinded readers, including those of four infants with severely abnormal scans. The most predictive abnormality in terms of subsequent MTS was an abnormal hippocampal $T_2$ signal. Of the eight children with prolonged febrile seizures who had two or more scans, four children had severe $T_2$ signal abnormalities

on their initial MRIs. Three of these four patients went on to develop anatomic evidence of MTS, although, to date, in only one has TLE developed. None of the other children has subsequent anatomic evidence of MTS. The preliminary data also indicated that recovery from hippocampal atrophy can occur in some of these children.

It is tempting to use imaging as a surrogate for clinical outcome, but the approach should be used with caution. The data available so far demonstrate that very prolonged febrile seizures can result in acute hippocampal injury and subsequent MTS. They do not tell us how often this occurs or how often it results in subsequent medically refractory TLE. It is clear that not all cases of MTS are associated with refractory TLE[126,127] .It also is clear that only a minority of cases of MTS or TLE are associated with prior febrile seizures, whether causally or otherwise[102,109,110,118,122,128] . Despite the limitations, imaging studies offer the best opportunity to address directly the relation between febrile seizures and MTS in the human. The recent development of good animal models of febrile seizures gives additional insight into the possible relation of prolonged febrile seizures and subsequent MTS and TLE [102].Recent animal data from Baram and colleagues[102,129] suggest that prolonged febrile seizures may lead to long-lasting changes in the hippocampal circuits. In a rat model of prolonged febrile seizures,

cytoskeletal changes in neurons were evident within 24 hours and persisted for several weeks without leading to cell loss. However, altered functional properties of these injured neurons were evident and persisted over the long term (<60 days)[102,130] .The changes were unique to prolonged febrile seizures and were not seen in other models of prolonged seizures in the immature brain. In the model developed by Baram and colleagues[102,129], although transient anatomic changes occurred, no evidence of cell death was found after prolonged febrile seizures. Remarkably, although this research has produced convincing data for functional changes, seizure duration of 20 minutes or more was required. Seizures lasting 10 minutes or less were not associated with any anatomic or functional changes. The availability of animal models provides a new means of studying the pathophysiology of febrile seizures and their consequences.

Additional issues that should be addressed include the role of preexisting neurologic abnormalities, effects of genetic background, and possible associations with specific viral infections.

**The Role of Preexisting Abnormalities in Seizure Induced Injury**

Whereas it is clear that seizure-induced injury can occur in humans, the necessary substrates have not been identified. The clinical[121-123] and

animal[131] data suggest that children with preexisting brain abnormalities may be more prone both to having prolonged seizures and to seizure-induced injury. In the study of VanLandingham et al. [123] , two of three children who demonstrated acute hippocampal changes that progressed to MTS had evidence of preexisting pathology. A high frequency of subtle cortical dysplasia[119,132] or other preexisting hippocampal abnormalities exists in patients with evidence of MTS. Moreover, animal data indicate that rat pups with cortical dysplasias are more prone to seizure-induced damage[131].Further studies are needed to clarify whether preexisting MRI abnormalities are an independent risk factor for hippocampal injury in humans or if they simply predispose to prolonged and lateralized seizure activity, which then causes the damage.

**Genetics**

Accumulating evidence indicates that a genetic contribution may exist to susceptibility to febrile seizures, susceptibility to prolonged seizures, and even susceptibility to seizure-induced damage. It has long been known that a family history of febrile seizures is a major risk factor for febrile seizures in offspring.[102]More recently, research demonstrated an underlying predisposition to prolonged seizures. Although children with a prolonged first febrile seizure are not at increased risk for another febrile seizure,

should one occur, it is likely to be prolonged [115].The same is true in children with a first unprovoked, prolonged afebrile seizure[133] .A clear genetic component to prolonged seizure was demonstrated in twin studies by Corey et al.[134] The researchers reported a risk of SE of 38% (55% when the co-twin also had a history of seizures) among the co-twins of monozygotic twins who experienced SE. The recent report of an association between a polymorphism at the interleukin-1β (IL-1β) locus and MTS in patients with TLE suggests that genetic factors also may predispose to the development of MTS after a prolonged febrile seizure[135]. IL-1β has been implicated in the mechanism of generating fever, in lowering the seizure threshold, and in prolonging seizures[102] .However, in spite of all the tantalizing hints regarding possible genetic factors in the occurrence of febrile seizures and of seizure-induced injury, little is known about the precise genes involved or the mechanism by which their influence might be exerted. The genetic mechanisms involved in the susceptibility to febrile seizures, in general, and prolonged febrile seizures, in particular, as well as the genetic mechanisms responsible for predisposing to seizure-induced injury, each offer exciting avenues of future research.

**Role of Specific Pathogens**

Several lines of evidence demonstrate that specific viral pathogens, in particular, human herpes virus (HHV)-6 and HHV-7, may be implicated in the development of MTS after prolonged febrile seizures. Findings in the pediatric literature implicate HHV-6 and HHV-7 in up to half the cases of febrile seizures in children younger than 3 years[136,137] .Children with primary HHV infection are more likely to have prolonged, focal febrile seizures and to have postictal paralysis than are those patients with febrile seizures not occurring with HHV-6 infection. It remains unclear whether these viruses are associated with prolonged febrile seizures because of the high fevers that occur with them or whether the viruses are involved with the pathogenesis of seizure-induced damage, as the herpesviruses have the potential to be neurotropic[138] .

## 2.7 CHRONIC TLE EPILEPSY

Patients with temporal lobe epilepsy (TLE) were significantly more likely to have recurrent seizures than were those with extratemporal or generalized epilepsy. O'Brien et al[139]reported progressive hippocampal atrophy over a 4-year period in a 28-year-old man with intractable TLE of long-standing duration.

Some studies suggest that patients with TLE and normal MRI are less likely to have cognitive deficits compared with those with atrophy of mesial structures.[140] Whether this remains true in extratemporal or generalized epilepsies may not follow these rules. For example, Mirsky et al. [141]demonstrated disturbances in attention in a group of children with absence seizures. Furthermore, Janz[142] reported a higher frequency of psychiatric disturbances in patients with juvenile myoclonic epilepsy compared with controls. Finally, the absence of structural changes is not necessarily predictive of a good seizure outcome, as intractable epilepsy in patients with normal MRI studies is recognized in most epilepsy surgical programs. Paradoxically, the absence of atrophic hippocampal volumes in intractable TLE is predictive of a less favorable postsurgical seizure outcome than in those with MTS[143] .

The quantification of human piriform cortex and cortical amygdala (PCA) volume with MRI showed that the PCA is extensively damaged in chronic TLE patients, particularly in those with hippocampal atrophy.[144]

## 2.8 Investigations:

**2.8.1 Imaging Studies:** Noninvasive imaging modalities are playing an increasingly important role in the evaluation of patients for epilepsy surgery.

A classic example is the visualization of mesial temporal sclerosis (MTS) on MRI, which has simplified the identification of patients who might benefit from anteromesial temporal lobectomy. Nevertheless, roughly 30% of patients with electrographic evidence of temporal lobe epilepsy have normal MRI scans[145]. The location of the seizure focus is unclear in this patient population. Possibilities include (a) a subtle form of MTS that is not apparent on MRI; (b) other pathology of the medial temporal lobe not visible on MRI, such as microdysgenesis or alterations in synaptic or receptor physiology; or (c) temporal neocortical pathology not detected by MRI, such as certain forms of cortical dysplasia. Distinguishing between these potential etiologies is critical to selecting the appropriate surgical target to ensure optimal seizure control and to minimize the potential neuropsychological sequellae of removing nonepileptic, functional tissue.

One possible solution would be to implant invasive electrodes in patients with temporal lobe epilepsy and a normal MRI scan. In fact, this treatment plan is the standard of care in some centers[146]. However, the implantation of subdural grid and depth electrodes is not without morbidity, and avoiding this increased risk, as well as cost and length of stay for the patient, would be preferable if outcome were not compromised.[147,148] Another approach would be to eliminate these patients from consideration

for surgery altogether, because their seizure-free rate is less than that of patients who have clear evidence of hippocampal atrophy or high signal on preoperative MRI.[149] This practice would deprive a large number of patients, who potentially could be cured of their epilepsy, from surgical therapy. Another option is to use additional information, such as history or video-EEG monitoring, to determine who might benefit from surgery without requiring the use of invasive electrodes.[150,151]

Interictal positron emission tomography (PET) with [$^{18}$F]fluorodeoxyglucose (FDG-PET) hypometabolism is known to lateralize the side of seizure onset in patients with mesial temporal lobe epilepsy and correlates well with seizure control after surgery .[152] In this study, Carne et al. attempted to use PET scans to try to identify a subgroup of patients with normal MRI scans who might benefit from temporal lobectomy. They found that 87% of patients with normal MRI scans had PET hypometabolism that was lateralized concordant with their EEG (compared with 100% of patients with MTS on MRI). In addition, 66% of these scans had more widespread hypometabolism in the temporal lobe than in a control group of patients with MTS, for whom the hypometabolism was more focal in the mesial structures. Unfortunately, the surgical approach was not uniform, and half of the 20 MRI-normal patients had a standard anterior temporal lobectomy and

amygdalohippocampectomy (the authors do not define the extent of neocortical resection), whereas the other half had a hippocampal-sparing neocortical resection guided by the extent of PET hypometabolism. The surgical results were extremely good, with an 80% rate of Engel Ia or Ib after a minimum follow-up of 2 years, regardless of the type of surgery performed.

The authors conclude that patients with MRI-negative temporal lobe epilepsy and concordantly lateralized PET scans, with widespread temporal lobe hypometabolism, are a unique group that likely has neocortical onsets and can benefit from neocortical resections. However, in spite of their good results, this conclusion is questionable because some of the data are inconsistent. The authors propose using PET scans to differentiate a subtype of patients with MRI-negative temporal lobe epilepsy, but they do not describe a comparison group of patients in whom the PET is either nonlateralized or more focally mesial that are in any way different from the rest of the study group. The authors point out that two patients with nonlateralized and one with a contralaterally lateralized PET scan were all rendered seizure free after surgery. Hence, the value of the PET scan in their decision making is unclear, and the predictive value of the PET scan results is not discussed. In addition, the authors never address the possibility that

patients with normal MRI scans can actually have strictly mesial temporal lobe onsets. This omission is clearly misleading, because a subgroup of these patients can be cured after selective mesial temporal surgery. Finally, the value of removing the neocortical tissue to the extent of the PET abnormality seems unjustified, because even patients with MTS and strictly mesial onsets often have regions of PET hypometabolism that extend far beyond the margins of the epileptic focus.[153]

**2.8.2 EEG:**

Interictal EEG should be performed in all patients with suspected TLE.Interictal abnormalities, consisting of spike/sharp and slow complexes, usually are located in the anterior temporal region (F7/F8 and T3/T4 electrodes) or basal temporal electrodes (T9/T10 and F9/F10). One third of patients with TLE have bilaterally independent, temporal interictal epileptiform abnormalities.Ictal recordings from patients with typical TLE usually exhibit 5-7 Hz, rhythmic, sharp theta activity, maximal in the sphenoidal and the basal temporal electrodes on the side of seizure origin.

In documented temporal lobe seizures, lateralized postictal slowing, when present, is a reliable lateralizing finding.Video-EEG telemetry is used as part of the presurgical evaluation. It also is used if the diagnosis of TLE is

suspected but still in question.Intracranial EEG with placement of intracranial subdural electrodes is done only if the patient is a surgical candidate and MRI and other non-invasive EEG data are not sufficiently localizing.

## 2.9 Medical Care:

The newer AEDs, such topiramate, lamotrigine, levetiracetam, oxcarbezapine, and zonisamide have similar if not better efficacy than the older AEDs. In patients with newly diagnosed epilepsy, lamotrigine appears to be significantly better than carbamazepine in terms of tolerability and health-related quality of life issues[154].

## 2.10 Surgical Care:

Refractory Familial Mesial Temporal Lobe Epilepsy (FMTLE) patients have good surgical outcome when unilateral or clearly asymmetric hypocampal atrophy is identified. Preoperative investigation should be the same as that in patients with sporadic refractoryTLE.[155]

Anterior temporal lobectomy:

Temporal lobectomy is the definitive treatment for medically intractable TLE .When seizures are not controlled by 2 different AED trials,

the patient should be considered for a presurgical evaluation. These patients are not likely to achieve seizure control with medications alone (5-10% chance of becoming seizure free[156].

The presence of unilateral hippocampal sclerosis and concordant EEG findings predict seizure-free outcome in patients considered for surgery. Foldvary and colleagues showed that a higher monthly preoperative seizure frequency is associated with a less favorable surgical outcome[157].

An extensive presurgical assessment for the feasibility of surgery is essential. This includes MRI, interictal and ictal EEG, neuropsychological testing, and the intracarotid amobarbital test.[158]

Seizure-free state at 2 years postoperatively is predictive of long-term seizure-free outcome. In well-selected cases, 70-80% of patients with refractory TLE become seizure free after surgery.[159]

**2.11 Prognosis:**

Sudden unexplained death in epilepsy (SUDEP) has been reported to be 24 to 40 times higher than that in the general population, with estimates ranging between 1 in 200 and 1 in 1,000. SUDEP accounts for 7% to 17% of deaths in the general population of patients with epilepsy, and for up to 50% of deaths in patients with refractory epilepsy.[160-163] Between 5% and 15% of

SUDEPs have been attributed to autonomic dysfunction that led to tachyarrhythmias in most cases, although bradyarrhythmias and episodes of cardiac asystole also have been reported.[164,165]

Hilz et al. demonstrate a reduction of sympathetic cardiovascular modulation and baroreflex sensitivity after anterotemporal lobectomies in 18 patients with pharmaco-resistant temporal lobe epilepsy (TLE). Such changes in sympathetic autonomic function are thought to minimize the risk of sympathetic-mediated cardiac arrhythmias as well as extreme bradycardic counter- regulations, two pathogenic mechanisms thought to be operant in SUDEP. Most of these cardiac arrhythmias have been directly attributed to ictal activity (more often during generalized tonic–clonic seizures). Hilz et al., however, citing data from experimental studies done in animals, also suggest a pathogenic role of interictal epileptic discharges through an enhancement of the sympathetic tone. Other authors have suggested that intense sympathetic stimulation after recurrent seizures can cause a nidus of myocardial irritability during periods of prolonged cardiac repolarization (evidenced by long QT intervals).[166] Such processes eventually result in "cardiac electrical instability" that can be reversed after surgical treatment. For example, in a study of 15 patients with refractory TLE who underwent an anterotemporal lobectomy, Frysinger et al.[167] found wider variations in

heart rate (measured with spectral plots of the RR interval) among patients with persistent seizures after surgery than in seizure-free patients and controls. Eventually, pathologic evidence of these disturbances can be identified in the myocardium of victims of SUDEP. Falconer and Rajs[168] described minor areas of fibrosis and scarring in the myocardium of nine victims of "epilepsy deaths." It is clear, therefore, that the impact of epilepsy surgery reaches beyond seizure remission. It reduces the risk of SUDEP in a patient population where its prevalence is not insignificant.

# Objectives

This study was performed to determine the clinical presentation, electro- encephalography abnormalities & MRI findings of patients with temporal lobe epilepsy.

# Methodology

This is a prospective (20 patients) and a retrospective (13 patients) cross sectional descriptive hospital based study conducted in Khartoum area neurological tertiary hospitals and referred clinics (Elshaab&Omdurman hospitals).

The study period was between June 2004-February 2005.

33 patients, who were given already a diagnosis of temporal lobe epilepsy on base of history &clinical examination supported by EEG&MRI, were studied.

These patients were reviewed according to a clinical protocol consisting of structured questionnaire (appendix), the following features in the history were particularly noted:-

Age of the patient, his sex ,age at onset ,duration of epilepsy, event duration and its frequency, details of any aura , characteristics of seizure whether it was simple or complex partial , subsequent of evolution , symptoms of increased intra-cranial pressure , motor or cranial nerve affection ,past history of central nervous system infection , febrile convulsion and family history of epilepsy. Because patients usually have only limited awareness of their behaviors during a seizure, additional in-

formations usually were obtained from family members and other close observers.

Clinical examination was conducted by me and other neurologist who used to see the patient, noting for general, cardiac, respiratory, abdominal and detailed neurological examination.

Investigations done include blood urea and electrolytes, urine analysis , serum calcium , 2hours post prandial blood glucose level and complete blood count in some patients when indicated.

EEG & brain MRI were requested to all patients and reported by expert radiologist and electroencephalographer.

The inclusion criteria to diagnose TLE were based upon:

- The repeated stereotypic occurrence of the same experience.
- Recurrent aura leading to complex partial or secondary generalization seizure.
- Or disappearance of the recurrent clinical phenomena with the use of anti-convulsants.

The diagnosis was supported by focal EEG changes or MRI finding.

There were no exclusion criteria.

Verbal consent was taken from each patient.

After designing the master sheet, all variables were introduced into the computer using D-base III for data entry .Consistency checked and analysis was carried out using Statistical Package for Social Sciences (SPSS).

Some patients found difficulty in performing EEG & brain MRI, they cost 65,000 Sudanese Dinars, and this obstacle was solved by doing them through Diwan Elzaka.

# Results

33 patients who had a confirmed diagnosis of temporal lobe epilepsy were included in the study .The mean age was 31, the median was 27,the mode was17,the standard deviation was18.34, six patients were identified at age group below 15 years of age, thirteen patients were in age group (16 – 30), seven patients were in age group (31 – 45), four patients were in age group (46 – 60) and only three patients were between (61 – 75) years. The youngest patient was seven years and the eldest was seventy years.( Figure1)

Sixteen patients (48.5%) had their disease onset before 15 years of age while eight patients their first seizure occurred at age group (16-30) and a similar number of patients had their fits for the first time at age group (31-45) and only one patient at age group (46-60) (Table 1).

Total of 33 patients studied eighteen patients (54.5%) were males, while fifteen patients (45.5%) were females. Male: Female ratio was 1.1:1 ,the difference statistically was not significant.( Figure 2).

Regarding the types of auras, the olfactory aura was found to be the most common form of aura (seven patients), three patients had a visual aura, four patients had a gustatory aura, six patients had an auditory aura, two patients had aura in from of fear, two patients had anxiety, four patients had

dizziness and one patient had distortion of body image. Four patients didn't report any type of aura.( Figure3).

Complex partial seizures was found to be the most common type of seizure among our study population occurring in twenty six patients, while simple partial was found in just seven patients .(Table 2).

In eleven patients their partial seizures evolve to secondary generalization.( Figure 4).

Five patients were accepted as having a validated past history of febrile conclusions.( Figure 5).

Total of (13 patients) had additional focal neurological symptoms in form of cranial nerves affection (3patients), five patients had symptoms of increased intra cranial pressure in form of headache and five patients had weakness. Clinical examination confirmed the presence of these focal neurological signs (Table 3 )&( Figure 6).

Just three patients reported a past history of acute central nervous system infection (meningitis or encephalitis).(Table 4).

Family history of epilepsy was reported in nine patients. (Table 5).

Inter – ictal EEG abnormalities were found in twenty seven patients, while six patients showed normal EEG. (Table 6 ).

The MRI findings among the study population showed three patients had tumors, one patient's MRI showed brain abscess spreading from otitis media, only one patient had hippocampus sclerosis, two patients had temporal infraction, one patient had an evidence of encephalitic changes and only one MRI showed arterio – venous malformation, while most of the study population (24) patients had no abnormality in their MRI.( Table 7).

**Table 1**
**shows age of onset of 33 Sudanese patients with Temporal Lobe Epilepsy**

| Age at Onset Groups | Frequency | Percent % | Valid Percent% | Cumulative Percent % |
|---|---|---|---|---|
| <15 | 16 | 48.5 | 48.5 | 48.5 |
| 16 – 30 | 8 | 24.2 | 24.2 | 72.7 |
| 31 – 45 | 8 | 24.2 | 24.2 | 97.0 |
| 46 – 60 | 1 | 3.0 | 3.0 | 100.0 |
| Total | 33 | 100.0 | 100.0 | |

**Table 2**
**shows types of seizure in 33 Sudanese patients with Temporal Lobe Epilepsy**

| Type of Seizure | Frequency | Percent |
|---|---|---|
| Simple | 7 | 21.2 |
| Complex | 26 | 78.8 |
| Total | 33 | 100.0 |

**Table 3**
**shows types of neurological symptoms among 33 Sudanese patients with Temporal Lobe Epilepsy**

| Abnormality | Frequency | Percent |
|---|---|---|
| Cranial Nervous Symptoms | 3 | 9.1 |
| Symptoms of increased I.C.P. | 5 | 15.2 |
| Weakness | 5 | 15.2 |

**Table 4**
**shows past history of acute CNS infection among 33 Sudanese patients with Temporal Lobe Epilepsy**

| Past History of CNS Infection | Frequency | Percent |
|---|---|---|
| Yes | 3 | 9.1 |
| No | 30 | 90.9 |
| Total | 33 | 100.0 |

**Table 5**
**shows family history of epilepsy among 33 Sudanese patients with Temporal Lobe Epilepsy**

| Family History of Epilepsy | Frequency | Percent |
|---|---|---|
| Yes | 9 | 27.3 |
| No | 24 | 72.7 |
| Total | 33 | 100.0 |

**Table 6**
**Shows presence of EEG abnormalities among 33 Sudanese patients with Temporal Lobe Epilepsy**

| EEG Abnormality | Frequency | Percent |
|---|---|---|
| Yes | 27 | 81.8 |
| No | 6 | 18.2 |
| Total | 33 | 100.0 |

**Table 7**

**Shows types of MRI abnormalities among 33 Sudanese patients with Temporal Lobe Epilepsy**

| Abnormality | Frequency | Percent |
|---|---|---|
| MRI Tumor | 3 | 9.1 |
| MRI Abscess | 1 | 3.0 |
| MRI Hippocampal Sclerosis | 1 | 3.0 |
| MRI Temporal Infarction | 2 | 6.1 |
| MRI Encephalitis Changes | 1 | 3.0 |
| MRI Arterio Venous Malformation | 1 | 3.0 |
| Normal MRI | 24 | 72.8 |
| Total | 33 | 100.0 |

**FIG (1) SHOWS AGE DISTRIBUTION OF 33 SUDANESE PATIENTS WITH TEMPORAL LOBE EPILEPSY**

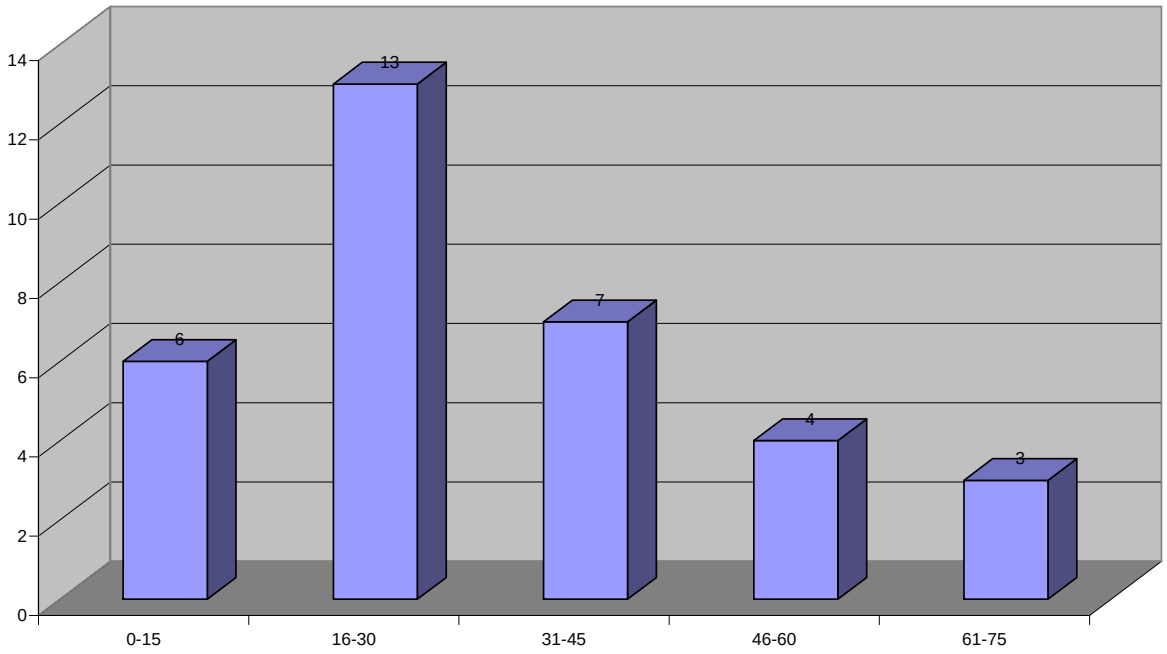


FIG (2) **SHOWS SEX DISTRIBUTION OF 33 SUDANESE PATIENTS WITH TEMPORAL LOBE EPILEPSY**

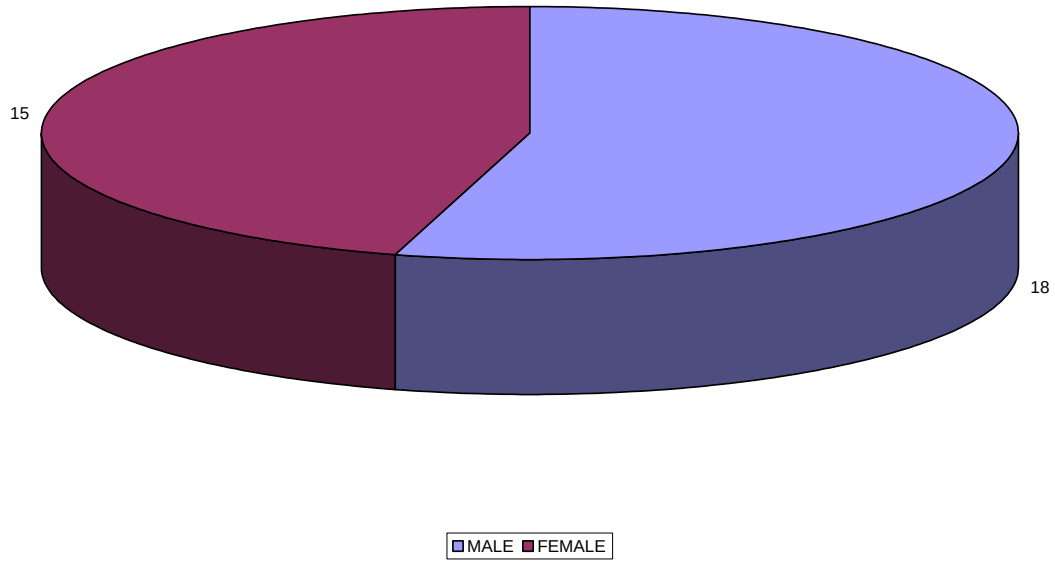


FIG (3) **SHOWS TYPES OF AURAS AMONG 33 SUDANESE PATIENTS WITH TEMPORAL LOBE EPILEPSY**

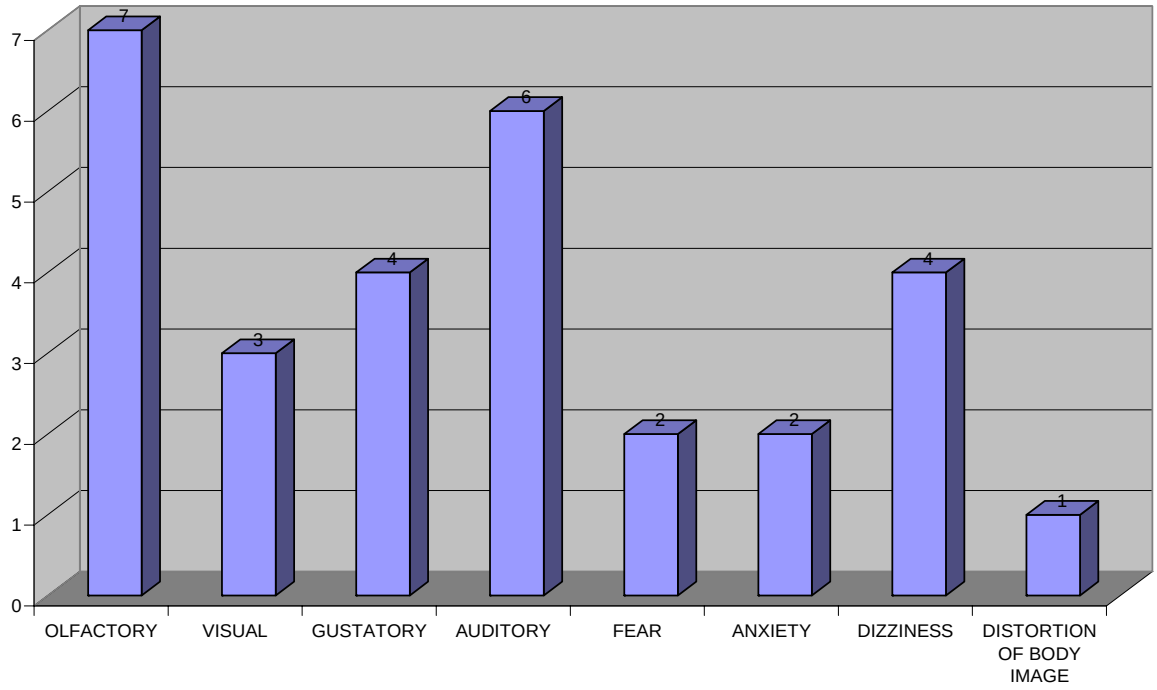


FIG (4) **SHOWS PRESENCE OF SECONDARY GENERALIZATION AMONG 33 SUDANESE PTIENTS WITH TEMPORAL LOBE EPILEPSY**

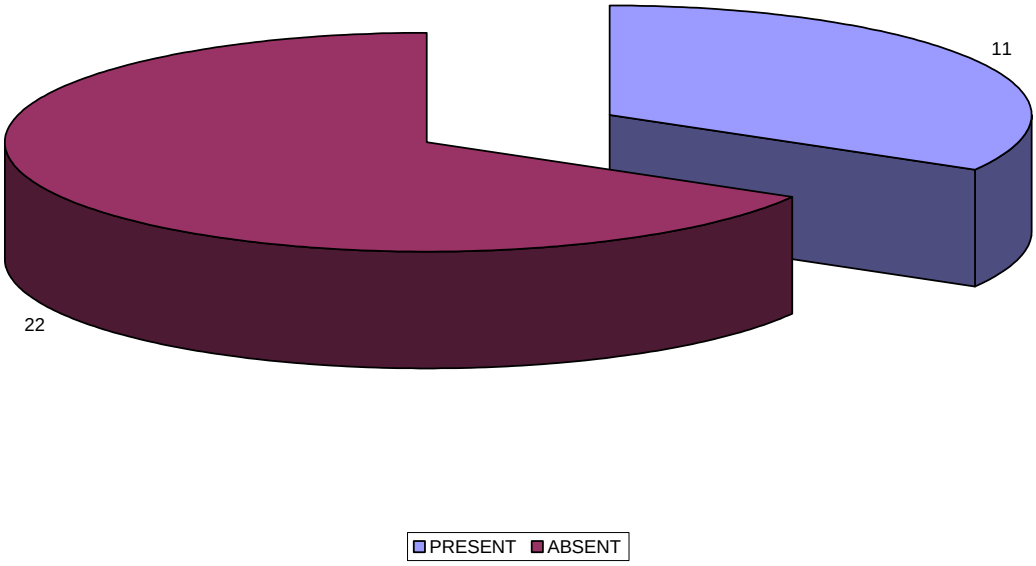


FIG (5) **SHOWS PAST HISTORY OF FEBRILE CONVULSIONS AMONG 33 SUDNESE PATIENTS WITH TEMPORAL LOBE EPILEPSY**

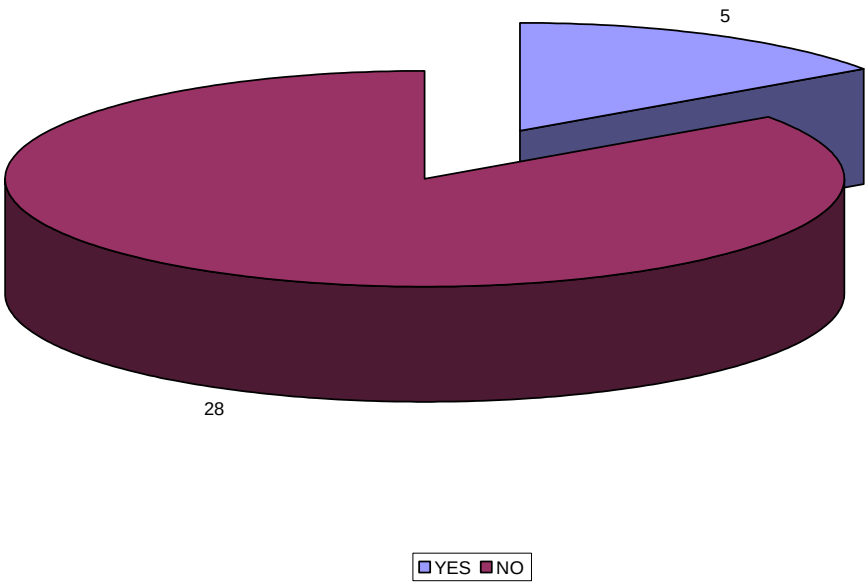
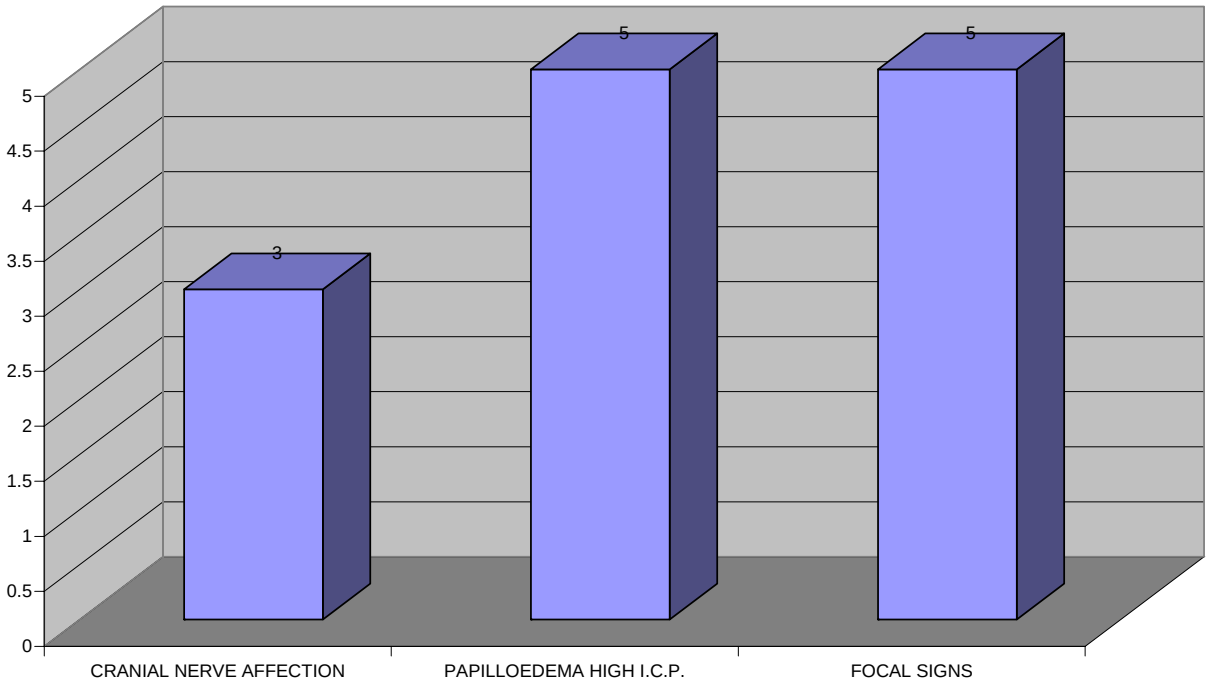


FIG (6) **SHOWS THE INCIDENCE OF ABNORMAL NEUROLOGICAL FINDINGS AMONG 33 SUDANESE PATIENTS WITH TEMPORAL LOBE EPILEPSY**



# Discussion

This study intended to describe the clinical, electroencephalographic and MRI findings in 33 patients with temporal lobe epilepsy.

There had been no similar studies done for this study population in specific, although numerous studies done in epilepsy as a general were published. a full detailed history from the patients and witnesses and proper clinical examination are mandatory for diagnosing temporal lobe epilepsy, because it is a border land between neurology and psychiatry frequently come to the attention of psychiatrist and since symptoms may occur in the absence of generalized grand-mal seizures ,physicians may fail to recognize the epileptic origin of seizures, so misdiagnosis and failure to diagnose TLE are common. A prospective study of 300 older children and adults with a first seizure a syndrome diagnosis could be made in 80%: clinical details plus family history allowed diagnosis in 47%, EEG allowed diagnosis in an additional 30%, and plus MRI allowed diagnosis in another 4%.[31]

The diagnosis of partial epileptic seizures is often challenging. The problem is considerable; the lifetime prevalence of epilepsy is 3-4%, and 60% of those affected have simple or complex partial seizures.[169,170]

In this study most of the study population had their seizure onset at childhood. Epilepsy is a common neurological disorder in childhood[171] and can have a major impact on a child's development.[172,173] In many children the seizures remit,[174] but in others the disorder continues and may affect adult life.[175]

Childhood epilepsy requires integrated medical, educational, and community services, and its treatment spans acute and disability medicine.

There are many childhood epilepsies, and seizures are the commonest pediatric neurological symptom. Epilepsy—that is, susceptibility to continuing seizures—occurs in 0.5-1.0% of the population and is intractable to current antiepileptic drug treatment in 20-25%. Epileptic seizures, including febrile convulsions, occur in 3-5% of children. Epilepsy starts in childhood in 60% of cases, and most of the clinically significant aspects of the disease occur during childhood.[176]

Only three patients were above age of sixty. Old age is the most common time in life to develop epilepsy.[50] More than 11 million elderly people live in the United Kingdom, at least 1% of whom will have epilepsy. Compared with younger populations, elderly people are more prone to develop seizures, whether provoked or unprovoked seizures. Seizures secondary to acute

central nervous system infections occur more commonly in developing countries than in developed countries.

Previous stroke is the most common underlying problem, accounting for 30-40% of all cases of epilepsy. Asymptomatic cerebral infarction can also lead to epilepsy, and, paradoxically, seizures may be a marker of increased risk for subsequent stroke.[56]Up to 70% of seizures are of focal onset, with or without secondary generalisation.[55]

Elderly people are, however, more susceptible to the adverse effects of drugs than their younger counterparts because the pharmacokinetics and pharmacodynamics of antiepileptic drugs differ in old age from those in younger patients.[61]

Most of our patients are males, this is most properly due to the fact that epilepsy is considered as stigma in our society & females tend to seek anon medical advice especially in certain diseases like in temporal lobe epilepsy (psychomotor epilepsy). [76]

The most common type of aura was found to be the olfactory aura .Acharya et al found that olfactory auras are associated more commonly with temporal lobe tumors than with other causes of TLE.[177]

The patho-physiology of aura is controversy. Partial and generalized seizures often affect autonomic function during seizures as well as during the interictal and postictal periods. Activation or inhibition of areas in the central autonomic network can cause cardiovascular, gastrointestinal, cutaneous, pupillary, urinary, and genital manifestations. Autonomic dysfunction during or after seizures may cause cardiac and pulmonary changes that contribute to sudden unexplained death in epilepsy.[178]

Most of our patients had complex partial seizure; some times temporal lobe epilepsy is called complex partial seizure. Overall incidence figures show that partial (focal) seizures (simple and complex) are the most abundant seizure type, accounting for more than 50 percent of all seizures; complex partial (focal seizures with alterations of awareness or consciousness) are the most common[6].

One third of our patients their seizures evolve to a secondarily generalized seizure. Large consecutive case series indicate that many people presenting with a dramatic first generalised tonic-clonic "grand-mal" seizure have had previous, undiagnosed simple or complex partial seizures (such as intense "deja-vu", a sudden feeling of fear, a bad smell or taste, or brief language difficulties), absence seizures, or epileptic myoclonus.[31] The first convulsive seizure may simply be the first recognised seizure pointing to the diagnosis

of epilepsy. Here we should emphasizes on the point that careful history should be taken from the witnesses to recognize whether the fits start focally then evolve to a secondarily generalized seizure or it is a primary generalized seizures.

Partial-onset seizures occur frequently during non-REM (NREM) sleep, especially stage two sleep. Frontal lobe seizures are most likely to occur during sleep. Patients with temporal lobe seizures have intermediate sleep seizure rates, and patients with seizures arising from the occipital or parietal lobes have rare sleep-onset seizures. Sleep, particularly stage 2 sleep, promotes secondary generalization of temporal and occipitoparietal, but not frontal, seizures. These findings suggest that the hypersynchrony of sleep facilitates both initiation and propagation of partial seizures, and that effects of sleep depend in part on the location of the epileptic focus.[179]

TLE is diagnosed predominately on clinical grounds mainly, whether there is doubt ,it maybe necessary to take the history(with witness accounts) over several visits. However, it is worth emphasizing that the diagnosis is usually made from the description of the episodes obtained from the patient or eyewitnesses, or both. This information is often, but not always, supported or supplemented by findings from electroencephalography.

In this study ,clinical examination detected additional neurological abnormalities ,e.g. cranial nerves palsies (II,VI, VII) and hemiplegia.

Clinical examination may add other focal neurological signs which may point to the underlying pathology such as brain tumor. Any patient with symptoms and signs of increased intra-cranial pressure like headache , vomiting , blurring of vision , papilloedema or focal neurological signs like hemiplegia; in addition to anew onset focal seizure ,structural temporal lobe lesion (like tumor ,infarction, A-V malformation) should be suspected and it's important to guide the neurologist to the most appropriate investigation ,here MRI is superior to EEG.

Five patients had past history of febrile convulsion. One of the most controversial issues in epilepsy research is whether prolonged febrile seizures cause mesial temporal sclerosis (MTS) and temporal lobe epilepsy (TLE). Retrospective studies from tertiary epilepsy centers report that many adults with intractable TLE have a history of prolonged or atypical febrile seizures in childhood. However, population-based studies have failed to confirm this association, as have prospective studies of febrile seizures.[102]

In most studies, the risk of developing epilepsy after simple febrile seizures is only mildly elevated compared with the risk for the general population[102-109]. To the contrary, complex febrile seizures are clearly

associated with an increased risk of subsequent epilepsy. Complex febrile seizures are febrile seizures that last longer than 15 minutes, have focal features, or recur within 24 hours[103].

Prolonged febrile seizures, particularly very prolonged febrile seizures and febrile status epilepticus (SE), are associated with a substantially elevated risk for future epilepsy.[102-105] However, not all children with febrile seizures in whom epilepsy develops will have TLE. Typically, in those patients with generalized febrile seizures, generalized epilepsies will develop, whereas in those individuals with focal febrile seizures, focal epilepsies will develop[102,104], suggesting that febrile seizures may be an age-specific expression of seizure susceptibility in patients with an underlying seizure diathesis[102,104,108].

Only three patients had a past history of meningitis or encephalitis. A population-based cohort of 714 survivors of encephalitis or meningitis between 1935 and 1981 was followed in order to evaluate the risks of unprovoked seizures after CNS infections. The 20-year risk of developing unprovoked seizures was 6.8%, and the ratio of observed to expected cases of unprovoked seizures was 6.9. The increased incidence of unprovoked seizures was highest during the first 5 years after the CNS infection but

remained elevated over the next 15 years of follow-up. The type of CNS infection and the presence or absence of seizures during the acute phase of the CNS infection greatly influenced the risks of subsequent unprovoked seizures. The 20-year risk of developing unprovoked seizures was 22% for patients with viral encephalitis and early seizures, 10% for patients with viral encephalitis without early seizures, 13% for patients with bacterial meningitis and early seizures, and 2.4% for patients with bacterial meningitis without early seizures. The 20-year risk of 2.1% for patients with aseptic meningitis was not increased over the general population incidence of unprovoked seizures.[180]

(27.3%) of the study population gave a family history of epilepsy. Only recently an inherited epilepsy syndrome with predominant auditory seizures has been identified in several families. These seizures are thought to originate in the lateral neocortical temporal cortex [181,182]. The syndrome was termed autosomal dominant partial epilepsy with auditory features. A mutation in one copy of the leucine-rich, glioma-inactivated 1 gene (LGI1) in the 10-cM region on chromosome 10 q24 was identified in some but not all families [183] associated with the syndrome. Seizures are characterized by prominent auditory hallucinations such as auras. Secondarily generalized seizures are common [184], and MRI findings are usually normal [182]. However,

others describe abnormalities of the temporal neocortex that can be visualized on MRI [185].

The diagnostic work will vary greatly in complexity, depending on response to medical treatment and consideration of surgical therapy. A careful history by an experienced examiner should establish the diagnosis of epilepsy and help define the seizure type. A routine EEG may or may not be helpful, as interictal abnormalities may be lacking. Interictal EEG would not be able to differentiate mesial from neocortical temporal origin, or even extratemporal origin. Special EEG analysis techniques might help [186]. Some times epilepsy is difficult to diagnose clinically; 20% of patients referred with intractable epilepsy prove to have pseudoseizures.[187] The false positive rates of properly reported EEG are 0.5%. [188,189] .

Most of the EGG reports were abnormal. Disappointingly, although it came as abnormal, the reports were fragmentary and there was no detailed analysis of them by the electro-encephalographer . The value of the EEG interpretation is related directly to the interpretive skills of the electroencephalographer. Only individuals with significant experience are able to recognize the characteristic features of a benign epileptic disorder and differentiate it from more serious syndromes.

Seizure frequency and epilepsy duration (years of patient's life with seizure activity) were independently associated with inter ictal discharge (IED) frequency, suggesting that (IED) are modulated by seizures.[190]

If a first seizure is unprovoked, large case series support the value of electroencephalography (EEG), and often magnetic resonance imaging (MRI), to identify the cause.[35,36] Such images cannot be used to diagnose the event—the diagnosis can only be made from the patient's history. The value of EEG is to point to focal lesions (especially localised slow waves), predict recurrence, and indicate a specific epilepsy syndrome (spike pattern). When performed within 24-48 hours of a first seizure EEG shows substantial abnormalities in about 70% of cases.[31,37] The yield may be lower with longer delays after the seizure. When standard EEG is negative, systematic case series have shown that sleep deprived EEG will detect epileptiform (spike) discharges in an additional 13-31% of cases.[31,37]

Only one patient's MRI showed hippocampal sclerosis, while twenty four reports were normal.The introduction of MRI permitted identification of hippocampal atrophy and signal-intensity change in patients with TLE who were being considered for epilepsy surgery.[93,94]

In pediatric epilepsy surgical series, approximately 20 percent of children younger than 12 years and 30 percent of children younger than 20 years have hippocampal sclerosis[191]. Most removed temporal lobes reveal prenatally acquired abnormalities of neurogenesis[192]. In the youngest surgical population (younger than three years), extra temporal lesions are the rule and hippocampal sclerosis is not seen[193]. By comparison, in adult multicenter data, 79 percent of surgeries were anterotemporal resections or amygdalohippocampectomies for non-lesional epilepsy, including hippocampal sclerosis[194] .

While not always available, MRI is the best method for structural imaging. Several case series comparing it with computed tomography in the same patient indicate that the latter may not detect small tumours or other subtle pathologies [31] After a first seizure, abnormalities detected by MRI that lead directly to intervention are more common in adults than children.[38] In a series of 166 adults with a first seizure, the most common aetiologies diagnosed with both computed tomography and MRI were cerebrovascular lesions (26%), brain tumours (12%), traumatic scar formations (5%), and other conditions (4%).[39]

In conclusion, the best imaging technique for looking at subtle temporal lobe pathology is the MRI, particularly in the hippocampus, a common site of seizure onset. Special thin cuts with nonstandard imaging angles are necessary to adequately assess hippocampal anatomy[22], but here in Sudan only standard MRI is available. This is, may be, why the majority of reports came as normal.

One of the newest MRI techniques useful in epilepsy is functional MRI. Using special MRI sequences, areas of specific brain function can be localized by imaging patients while they perform specific tasks. For example, areas of language function in the brain can be visualized by having the patient do language-related tasks during the scan. This information is often very useful to the neurosurgeon; the proximity of these areas to the seizure-causing region can be determined before surgery.

Epilepsy may present with a variety of symptoms, and other conditions may mimic its manifestations. The diagnosis is almost always based solely on the clinical history. It is therefore not surprising that diagnostic accuracy remains a major problem.[195] About a fifth of patients referred to specialist units with "intractable epilepsy" are found, on further assessment, not to have epilepsy.[196] It is also common for patients to have symptoms for

months or even years before epilepsy is diagnosed. Thus, it is important to be aware of both the heterogeneous and sometimes subtle forms of epilepsy and of the alternative diagnoses.[197]

Surgery has an increasing role in TLE .There must be many people suitable for such surgery ,not currently under specialist follow up, who are unaware of this potentially curative option.

future studies will hopefully be rewarding with large population size.

# Conclusion

The study showed that:

1/ Most of our study population were between (16 – 30) years of age.

2/ Age of onset of TLE was mainly in the childhood period.

3/ TLE can effect both sexes here males were affected more than females.

4/ Auras were common in patients with TLE especially olfactory aura.

5/ Most of patients had complex partial seizure.

6/ One third of patients had secondary generalization.

7/ Presence of focal neurological symptoms & signs raise the possibility of brain structural abnormality.

8/ Febrile convulsions and central nervous system infection during childhood were risk factors for developing TLE.

9/ (81.8%)of the study group had abnormalities in their inter-ictal EEG.

10/ only one patient showed hippocampal sclerosis in their MRI.

# Recommendations

1/ a full detailed history from the patients and witnesses and proper clinical examination are mandatory for diagnosis of temporal lobe epilepsy, because it resembles other psychological diseases and contains some psychic-phenomena.

2/ Inter-ictal EEG should be performed in all patients with suspected TLE.

3/High resolution MRI is the neuro-imaging modality of choice for patients with TLE especially if CT brain shows no structural abnormality like tumor abscess, infarction, or others.

4/ Febrile convulsions in children should be treated promptly to prevent further damage in later life.

5/Further studies with large number of patients should be done.

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