



# **Clinico-radiological Profile in Children with Drug Resistant Focal Epilepsy**

Thesis

*Submitted for Partial Fulfillment  
of Master Degree in Pediatrics*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

# قَالَ

لَسْبِحَانَكَ لَا يَلْمُ لَنَا  
إِلَّا مَا عَلِمْنَا إِنَّكَ أَنْتَ  
الْعَلِيمُ الْعَظِيمُ

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# List of Contents

Title	Page No.
List of Tables.....	5
List of Figures.....	6
List of Abbreviations.....	8
Introduction.....	- 1 -
Aim of the Work.....	13
Review of Literature	
▪ Drug Resistant Focal Epilepsy.....	14
▪ Management of Focal Epilepsy.....	27
Subjects and Methods.....	49
Results.....	55
Discussion.....	68
Summary.....	77
Conclusion.....	80
Recommendations.....	81
References.....	82
Arabic Summary	

# List of Tables

Table No.	Title	Page No.
<b>Table 1:</b>	MRI protocol optimized for the detection of epileptogenic lesions in early outpatient MRI performed in 1.5 Tesla MRI scanners .....	52
<b>Table 2:</b>	Showing a list of epileptogenic entities and the suitability of MRI sequences for their detection .....	53
<b>Table 3:</b>	Demographic & Seizure characteristics of the studied patients .....	55
<b>Table 4:</b>	Developmental History among studied cases .....	56
<b>Table 5:</b>	Localization of abnormality on EEG .....	59
<b>Table 6:</b>	Percentage of abnormal MRIs obtained using the old versus the new technique.....	61
<b>Table 7:</b>	Abnormalities identified using the novel MRI technique .....	62
<b>Table 8:</b>	Findings and abnormalities using the old and novel MRI techniques.....	63
<b>Table 9:</b>	Relation between EEG findings and Chalfont Seizure Severity Scale Score.....	65
<b>Table 10:</b>	Relation between Localization of abnormality on EEG findings and Chalfont Seizure Severity Scale Score .....	65
<b>Table 11:</b>	Relation between both Baseline & New MRI findings and Chalfont Seizure Severity Scale Score.....	66
<b>Table 12:</b>	Relation between abnormalities identified by new MRI and Chalfont Seizure Severity Scale Score .....	67

# List of Figures

Fig. No.	Title	Page No.
<b>Figure 1:</b>	ILAE 2017 classification of seizure types expanded version .....	15
<b>Figure 2:</b>	Hypothesized Biologic Mechanisms of Drug Resistance in Epilepsy .....	23
<b>Figure 3:</b>	Spike discharges at left central and mid-temporal region in a 6-year-old boy with a history of focal seizure involving the right arm .....	31
<b>Figure 4:</b>	Patient with drug resistant epilepsy due to cortical dysplasia .....	33
<b>Figure 5:</b>	Preoperative (A) and postoperative (B) coronal T2-weighted 3T magnetic resonance imaging (MRI) from a five-year-old boy with dual pathology .....	41
<b>Figure 6:</b>	Preoperative imaging from a 3-year-old girl with mild left hemiparesis, developmental delay, and multiple daily seizures .....	44
<b>Figure 7:</b>	<b>A:</b> The Vagus nerve is exposed on a rubber sheet. <b>B:</b> A helical electrode is successfully installed.....	46
<b>Figure 8:</b>	a, b Preoperatively, sagittal high-resolution and axial FLAIR MRI showed myelinated and slightly shorter corpus callosum. c, d Postoperatively, sagittal high-resolution and axial FLAIR MRI images .....	48
<b>Figure 9:</b>	Seizures types observed among cases.....	56
<b>Figure 10:</b>	Types of Generalized Seizures observed among cases .....	57
<b>Figure 11:</b>	Number of anti-epileptic drugs used by patients. ....	57

# List of Figures *cont...*

Fig. No.	Title	Page No.
<b>Figure 12:</b>	Patients with normal versus abnormal EEG findings.....	58
<b>Figure 13:</b>	Neurological examination of patients.....	59
<b>Figure 14:</b>	Occipitofrontal circumference in the patients' series.....	60
<b>Figure 15:</b>	Abnormality of neurological examination among patients.....	60

# List of Abbreviations

Abb.	Full term
<i>ABC</i>	<i>ATP-binding cassette</i>
<i>AED</i>	<i>Antiepileptic drugs</i>
<i>AIDS</i>	<i>Acquired immune deficiency syndrome</i>
<i>ATL</i>	<i>Anterior temporal lobectomy</i>
<i>BECTS</i>	<i>Benign childhood epilepsy with centrottemporal spikes</i>
<i>CD</i>	<i>Cortical dysplasias</i>
<i>CT</i>	<i>Computed tomography</i>
<i>DBS</i>	<i>Deep brain stimulation</i>
<i>DNET</i>	<i>Dysembryoplastic Neuroepithelial Tumor</i>
<i>DRE</i>	<i>Drug resistant epilepsy</i>
<i>DRFE</i>	<i>Drug-resistant focal epilepsy</i>
<i>EEG</i>	<i>Electro encephalogram</i>
<i>FCD</i>	<i>Focal cortical dysplasia</i>
<i>GABA</i>	<i>γ-aminobutyric acid</i>
<i>GERD</i>	<i>Gastroesophageal reflux disease</i>
<i>HMEG</i>	<i>Hemi megaloencephaly</i>
<i>ILAE</i>	<i>International league against epilepsy</i>
<i>KD</i>	<i>Ketogenic diet</i>
<i>LGS</i>	<i>Lennox-Gastaut syndrome</i>
<i>MEG</i>	<i>Magnetoencephalography</i>
<i>MRI</i>	<i>Magnetic resonance imaging</i>
<i>MRP</i>	<i>Multidrug resistance-associated protein</i>
<i>MRS</i>	<i>Magnetic Resonance Spectroscopy</i>

# List of Abbreviations *cont...*

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<b>Abb.</b>	<b>Full term</b>
<i>MTS</i> .....	<i>Mesial Temporal Sclerosis</i>
<i>NMDA</i> .....	<i>N-methyl-d-aspartate</i>
<i>PET</i> .....	<i>Position emission tomography</i>
<i>SAH</i> .....	<i>Selective amygdalohippocampectomy</i>
<i>SPECT</i> .....	<i>Single photon emission computed tomography</i>
<i>VNS</i> .....	<i>Vagal nerve stimulation</i>



## INTRODUCTION

**E**pilepsy is a disease associated with lasting derangement of brain function and predisposition to recurring seizures. It may arise from a variety of genetic, structural or metabolic causes. Seizures and epilepsy are generally divided into focal and generalized according to underlying cause or etiology (*Fisher et al., 2014*).

Partial (focal) seizures occur when electrical activity remains in a limited area of the brain. The seizures can sometimes turn into generalized seizures, which affect the whole brain. This is called secondary generalization (*Abou-Khalil et al., 2016*).

Partial seizures can be divided into simple partial seizures, which do not affect awareness, and complex partial seizures, which affect awareness or memory of events before, during, and immediately after the seizure (*Abou-Khalil et al., 2016*).

Drug-resistant epilepsy can be defined as the failure of adequate trials of two tolerated and appropriately chosen and used anti-seizure drugs (whether as monotherapy or in combination) to achieve sustained seizure freedom (*Nair, 2016*).

The causes of intractable focal epilepsy include cortical dysplasia, tuberous sclerosis, polymicrogyria, hypothalamic

hamartoma, Landau-Kleffner syndrome, and hemispheric syndromes, such as Sturge-Weber syndrome, hemimegalencephaly, and Rasmussen encephalitis and patients with epilepsy resulting from metabolic or degenerative problems (*Kossoff et al., 2003*).

The diagnostic modalities of intractable focal routine EEG, Long-term video-EEG monitoring, and neuroimaging such as MRI, Single photon emission computed tomography (SPECT), positron emission tomography (PET), functional MRI (fMRI) or Magnetoencephalography (MEG) tests (*Rosenow et al., 2015*).

Surgical intervention is a treatment modality of intractable focal epilepsy- regardless of age- in children who have persistent, frequent seizures that have an adverse impact upon their lives or are interfering with their cognitive and psychosocial development (*Steinbok et al., 2009*).

Surgical approaches can be divided into relatively less invasive procedures, such as vagus nerve stimulation; and surgeries such as focal resections, lobar or multilobar resections, corpus callosotomy hemispherectomy, and multiple subpial transections (*Steinbok et al., 2009*).

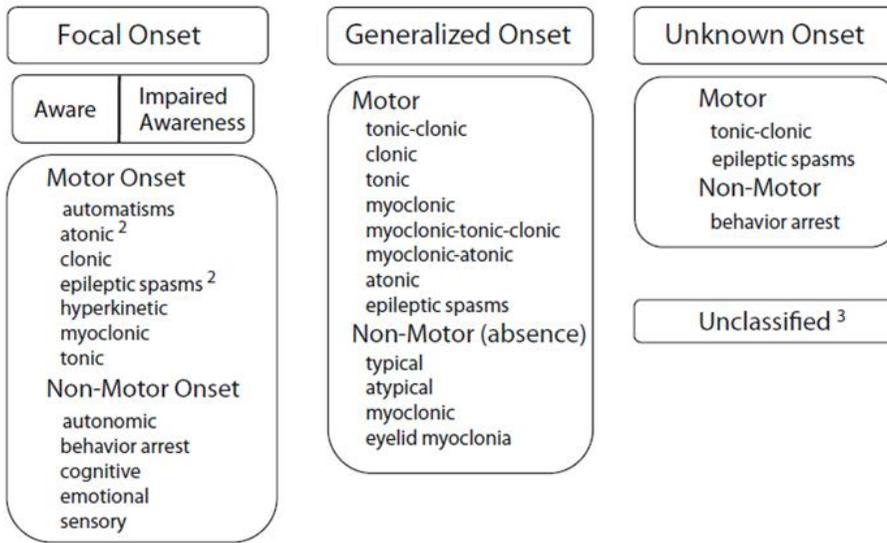
## **AIM OF THE WORK**

**T**he aim of this work is to identify patients with drug resistant epilepsy who have either persistent clinical focal seizures or persistent focal discharges on electroencephalogram (EEG), and to assess their clinical and neuroimaging findings, thereby deciding on their eligibility for epilepsy surgery.

**Chapter (1)****DRUG RESISTANT FOCAL EPILEPSY****Definition:**

**E**pilepsy is a chronic disorder characterized by a spontaneous tendency for recurrent seizures. Seizures are the clinical manifestation of abnormally hyper-excitabile cortical neurons (*Dey et al., 2016*). It is characterized by an enduring disposition towards recurrent unprovoked seizures. The diagnosis requires at least two seizures occurring greater than 24 hours apart or one seizure with a relevant abnormal electroencephalographic pattern or brain scan suggesting a high probability of a second seizure (*Fisher et al., 2014*).

A seizure is defined as a transient occurrence of signs and / or symptoms due to abnormal excessive or synchronous neuronal activity in the brain (*Fisher et al., 2005*).



**Figure 1:** ILAE 2017 classification of seizure types expanded version (Fisher et al., 2017).

### Etiology of Epilepsy:

Seizures are classified according to their aetiology as idiopathic (primary without a known cause), symptomatic (secondary) or cryptogenic. The brain disturbances responsible for the initiation of epileptic activity and seizures are also classified as either inherited or acquired (Berg et al., 2010).

Symptomatic epilepsy accounts for 25% to 45% of childhood epilepsy which is caused by known structural abnormalities or damage in the brain or an underlying disease (Bear et al., 2016).

Cryptogenic epilepsy ("kryptos" means "hidden") in which the child's epilepsy is symptomatic, but we cannot locate