Introduction

Epilepsy is a neurological disease that is characterized by paroxysmal, transient disturbance of the brain function, it may be manifested by episodic impairment of loss of consciousness, abnormal motor phenomena, psychic or sensory disturbance **(Hauser et al., 1997).**

Many conventional anticonvulsants are metabolized to generate reactive metabolites with capability of covalent binding to macromolecules. Therefore the anticonvulsants may not only suppress the epileptic spike but also elicit systemic toxicity through covalent binding of their metabolic intermediates to proteins or vital biomolecules. Peroxidation of membrane lipids caused by an increase in generation of free radicals or decrease in the activities of antioxidant defense systems has beensuggested to be critically involved in the seizure control **(Johanson et al., 1993).**

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The glutathione-s-transferases (GSTs) constitute a family of cytosolic isoenzymes that are involved in the detoxification of electrophilic xenobiotics. These enzymes also participate in the intracellular binding and transport of a broad range of lipophilic compounds including bilirubin and hormones such as glucocorticoids and thyroid hormones. By using immunohistochemistry, spectrophotometric enzyme essay, and reverse phase HPLC, it was found that GSTs were found in the neurons of the brainstem, forebrain and cerebellum, specific distribution was found in the cytoplasm, nuclei and nucleoli **(Hayes and Pulford, 1995).**

Cytosolic and membrane bound forms of GSTs are encoded by two distinct supergene families **(Board and Baker, 1997).** These enzymes are involved in the cellular defense against toxic, carcinogenic and pharmacologically active electrophilic compounds. At present eight classes of the soluble cytoplasmic GSTs are present (alpha, kappa, mu, omega, pi, sigma, theta, and zeta). These isoenzymes are found in a range of tissues and their expression has

significant biological and clinical implications including drug resistance and carcinogenesis **(Shang et al., 2008).**

Aim of the Work

The aim of the present study is to assess the serum level of GST as well as the plasma level of malondialdehyde (MDA) which is an index of extracellular lipid peroxidation in patients with epilepsy and study their relation to antiepileptic drug (AED) response .

Epilepsy

Definition:

Epilepsy is being defined as transient occurance of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain, usually self limitted. It is not a specific disease, but rather symptom complex secondary to abnormal brain function **(Fisher et al., 2005).**

Historical aspect:

The word epilepsy comes from a greek verb epilamranien (to be seized, to be taken hold, to be attacked), **(Engel and Pedely, 1997).**

The earliest description of tonic clonic seizures appear in egyptian hieroglyphic prior to 700 BC **(Fisch, 1996).**

The first known monograph on the subject is that by the Hippocrates about 400 BC in his book on the scared disease **(Keith, 1963).**

Epidemiology:

Prevelance:

Epilepsy is a highly prevelant disease, affecting 0.5-1.5% of the world's population**.** The overall prevelance of the epilepsies in childhood and adolescence 6-8 per 100**(Hauser, 1995).**

In Egypt, **El-Khayat et al., (1994),** studied the prevelance of epilepsy in primary school children and reported a prevelance of 3.5/1000. While, **Massoud (1997),** in his study of children of 195 primary schools in Cairo, reported even a lower overall revelance of 1.9/1000.

Age specific incidence:

The overall incidence of childhood epilepsy from birth to 16 years is approximately 40 in 100.000 children per year **(Camfield et al., 1996).**

Sex specific incidence:

Boys are 1-2.4 times more likely to have epilepsy than girls **(Levados et al., 1992).** Other studies found almost an equal sex incidence **(Freitag et al., 2001).**

Incidence by seizure type:

Generalized seizures and epilepsy syndromes are more prevelant in children 0-6 years of age, while partial types are prevelant in children aged 6-15 years **(Eriksson and Koivikko, 1999).**

Etiology of epilepsy:

Epilepsy has a wide range of causes and indeed almost all grey matter disease can result in seizures and the most important factor influencing the range of causes is age (**Shorvon, 2000)**.

The most common causes are:

(1) Local causes:

- Focal intracranial lesions as hematoma,cerebral abcess,intracranial tumours,and angioma.
- inflammatory conditions as meningitis,and encephalitis.
- degenerative and inborn errors of metabolism.
- trauma.
- phenylketonuria.
- Congenital abnormalities.
- Vascular diseases as intracranial heamorrhage, thrombosis, embolism, aneurysm and cerebral atheroma.

(2) general causes:

- Disordered metabolism:ureamia, hepatic failure, alkalosis, hypoglycemia, hypocalcemia.
- Endocrine disorders.
- -exogenous poisins: alcohol, cocaine, lead, insecticides.**(Lauders and Noachtar, 2001).**

Spectrum of epileptic seizures and syndromes

The international league against epilepsy (ILAE) classification of seizure type

I. Partial (focal) seizures

A. Simple partial seizures

1. With minor signs
   a) Focal motor without march
   b) Focal motor with march (Jacksonian)
   c) Versize
   d) Postural
   e) Phonatory
2. with somatory or special-sensory symptoms(simple hallucinations e.g.,tingling, buzzing,light flashes).
   a) somatosensory
   b)visual
   c)auditory
   d) olfactory
   e)gustatory
   f) vertiginous

3. with autonomic symptoms or signs (including epigastric sensation, pallor, sweating, flushing and pupilary dilatation).

4. With psychic symptoms; these symptoms rarely occur without impairement of consciousness and are much more commonly experienced as complex partial seizures

   a) Dysphasic

   b) Dynamic

   c) Cognitive

   d) Affective

   e) Illusions

   f) Structural hallucinations

B. Complex partial seizures

Simple partial onset followed by impairment of consciousness

a. with simple partial features followed by impaired consciousness

b. with automatism with impairment of consciousness at onset

   a. With impairment of consciousness

b. With automatisms

C. Partial seizures evolving to secondary generalized seizures

a. simple partial seizures evolving to generalized seizures

b. complex partial seizures evolving to generalized

c. simple partial seizures evolving to complex partial evolving to generalized seizures

II. Generalized seizures

a) Absence seizures

b) Myoclonic seizures

c) Clonic seizures

d) Tonic seizures

e) Tonic-clonic seizures

f) Atonic seizures

ILAE Commission report (1981)

The international classification of epilepsies and epileptic syndromes (Commission on classification and terminology of the ILAE, 1989).

Table (1): ILAE classification

Class	Classification
1.	Localization related (focal, local, partial)
1.1	Idiopathic (with age related symptoms)
	Benign childhood epilepsy with centrotemporal spikes
	Childhood epilepsy with occipital paroxysm
	Primary reading epilepsy
1.2	Symptomatic
	Chronic progressive epilepsia partialis continua of childhood
1.3	Cryptogenic
2	Generalized
2.1	Idiopathic (with age related onset, in order of age) Benign neonatal familial convulsions Benign neonatal convulsions Benign myoclonic epilepsy of infancy Childhood absence epilepsy (pyknolepsy) Juvenile absence epilepsy Juvenile myoclonus epilepsy (impulsive petit mal) Epilepsy with grand mal (GTC) seizures on awaking Other idiopathic generalized epilepcies with seizure precipitated by specific modes of activation
2.2	Symptomatic
	Non-specific etiology Early myoclonic encephalopathy Early infantile epileptic encephalopathy with suppression-burst Other sympyomatic generalized epilepsies not defined above
2.3	Specific syndromes
3	Epilepsies and syndromes undetermined whether focal or generalized
3.1	With both generalized and focal seizures Neonatal seizures Severe myoclonic epilepsy of infancy Epilepsy with continous spike waves during sleep Aquired epileptic aphasia (Landau-Kleffner syndrome) Other undetermined epilepsies not defined above
3.2	Without unequivocal generalized or focal features
4	Special syndromes
4.1	Situation-related seizures Febrile conculsions Isolated seizures or isolated status epilepticus Seizures due to acute metabolic or toxic factors such as alcohol, drugs, eclampsia

(Commission on classifications and terminology of the ILAE, 1989).

Clinical Presentations:

Childhood seizures happen when the electrical activity in child's brain is suddenly disrupted. This disruption can cause changes in child's body movements, awareness, behaviour, emotions or senses. There are many different types of seizure, each having their own set of symptoms, which often makes diagnosis difficult **(Simon et al., 2007)**.

The general symptoms of a seizure:

The child may have varying degrees of symptoms depending upon the type of seizure. The following are general symptoms of a seizure or warning signs that your child may be experiencing seizures. Symptoms or warning signs may include:

- Staring.
- Jerking movements of the arms and legs.
- Stiffening of the body.
- Loss of consciousness.
- Breathing problems or breathing stops.
- Loss of bowel or bladder control.
- Falling suddenly for no apparent reason.
- Not responding to noise or words for brief periods.
- Appearing confused or in a haze.
- Sleepiness and irritable upon waking in the morning.
- Nodding the head.
- Periods of rapid eye blinking and staring.

During the seizure, the child's lips may become bluish and breathing may not be normal. The movements are often followed by a period of sleep or disorientation **(Blum et al., 2002)**.

Differential diagnosis

Non-epileptic attacks include:

- **Vasovagal syncope:**

  loss of consciousness occurring in crowded trains, waiting at bus stops, or in school assembly; should always be presumed to be syncopal in nature unless there is clear-cut evidence to the contrary.

- **Night terrors:**

  These affect children aged between about 6 and 8 years, who suddenly awaken from a sound sleep, wide-eyed, screaming, and inconsolable. They are amnesic for the events the following morning. They seem to occur just as often in happy children as in children who are not doing well at school or in the family. Fortunately they, too, pass quickly.

- **Reflexic anoxic seizures:**

  Affect younger children, aged between 1 and 2 years. A typical story is of a child who has some minor injury, or who is crossed in some way so that he becomes suddenly

angry, upset, or frightened. Such attacks terminate spontaneously without treatment.

- **Febrile convulsions.**
- **Cardiac arrhythmias.**
- **Migraine.**
- **Narcolepsy (Neville, 1997)**.

Diagnosis:

Diagnosis of epilepsy involves four key stages:

- Recognition of the epileptic seizures.
- Classification of the seizure type(s)
- Identification of the epilepsy syndrome
- Identification of an underlying aetiology.

The clinical history and examination, form a part of the evaluation, but further investigation with electroencephalography, neuroimaging and other non-imaging tests, e.g. blood analysis, metabolic screening and muscle biopsy, are often required to obtain a complete picture. In general, the aims of these investigations are:

- To assist in identifying the epilepsy syndrome; and
- To identify any underlying aetiology, and thereby;
- Facilitate a prognosis; and
- Provide genetic counselling advice.

Imaging is not required in all children with epilepsy, but it plays a pivotal role in some cases. Making a diagnosis involves identifying a condition or disease based on signs and symptoms. The diagnosis itself is the actual term for the condition or disease **(Herzog et al., 2004)**.

Investigations:

Electroencephalography:

Because epilepsy is fundamentally a physiologic disturbance of brain function, the EEG is the most important laboratory test in evaluating patients with seizures. The EEG helps to characterize specific epileptic syndromes as well as helping in management and prognosis **(Pedley et al., 1995).**

Ictal EEG:

The EEG is invariably abnormal if recorded during the ictus, however , rarely in certain complex partial seizures,the surface EEG is normal but an abnormal pattern is seen if sphenoidal or depth electrodes are used **(Binnie, 1988).**

Interictal EEG:

The diagnostic value of an interictal EEG recording is one of the most abused investigations. It is often requested to exclude or to prove a diagnosis of epilepsy **(Binnie, 1988).**

Ambulatory EEG:

A portable cassette recorder is used to monitor the EEG continuously over prolonged periods. This allows detectiory of infrequent interictal localized discharges**(Morris, 1997).**