

## Etiologies of Adult Onset Epilepsy: Clinical and Paraclinical Study in the Governorate of Babylon.

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### ABSTRACT:

#### BACKGROUND :

Adult onset epilepsy (AOE) is considered the epilepsy that start after the age of 18 years. It is a common disorder, and it's etiology is variable from one place to another.

#### OBJECTIVE :

to study the etiologies, diagnosis and treatment of AOE in one governorate of Iraq and to compare it's different clinical and paraclinical abnormalities in different age groups.

#### PATIENTS & METHODS:

106 patients with AOE were enrolled in this prospective study, and included all patients who developed seizure after the age 18. The study was done in a heavy neurological clinic in north of Babylon governorate, Iraq, for 3 years from Sept. 2007 to Sept. 2010.

#### RESULTS:

A total of 102 patients met the criteria. Brain tumors were found in 24 (23.5%). No cause could be found in 25 (24.5%) of cases. Generalized tonic clonic seizure was registered in 47 patients (46%). EEG was positive in (57.3%) of cases and the MRI was conclusive in 63.7% of them.

#### CONCLUSION:

Brain tumors, CVD, post traumatic and inflammatory disease are the four major causes of AOE in Iraq. The most common type of seizure among different groups of etiologies of AOE is focal epilepsy.

**KEY WORDS:** epilepsy, seizure

### INTRODUCTION :

Epilepsy can occur at any age, and almost approximately 25% of patients with epilepsy will have their first seizure after the age of 25 years. These individuals will need special attention with regard to etiology. Brain tumors are one of several causes that may be suspected<sup>(1)</sup>. The main incidence and prevalence of adult onset epilepsy (AOE) is between 25-29 and older than 60 years<sup>(2,3, 4)</sup>.

In the united state the annual incidence of seizure is approaching 100 seizures per 100,000 in people aged over 60 year<sup>(5)</sup>. Etiology of AOE is variable from one nation to another and even from one place to another in the same nation. One of its most important causes is brain tumors, which has an incidence of epilepsy reaching approximately 30%<sup>(6)</sup>. Patients with slowly growing chronic lesions are more likely to have seizure disorder<sup>(6)</sup>. Another important cause of AOE is cerebrovascular disease (CVD). Seizure related to intracerebral hemorrhage occurs in 10.6% of cases, while those related to

ischemic stroke appear in 8.6 %<sup>(7)</sup>. Some authors have reported CVD as the most frequent cause of epilepsy in this age group and others have found tumors as the most common cause. Almost 25% of patient with infarction of cerebral cortex later develops recurrent focal or generalized epilepsy. According to surg and chu, previous infarcts are by far the most common lesions underlying status epilepticus in late adult life<sup>(8)</sup>.

Other important causes of AOE include: those that happen in the context of an acute insult to the central nervous system (CNS) or during an acute metabolic disturbances<sup>(9)</sup>. These seizures could be associated with subdural hematoma and CNS infections. They also can occur with systemic metabolic conditions such as uremia, hyperglycemia, hypoglycemia, hyponatremia and alcohol withdrawal.

Seizure as a result of Alzheimer and other degenerative disease are decidedly rare<sup>(10)</sup>. Some causes of epilepsy like alcohol with drawl are common in western world and it may reach up to 25% of cases of epilepsy in adult in certain countries<sup>(1)</sup>. In this study we try to determine the

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common etiologies, clinical and paraclinical features of AOE in Babylon governorate, one of the important and the biggest governorate in the middle Euphrates.

**PATIENTS AND METHODS:**

106 patients with AOE enrolled in this prospective study, and included all patients who developed seizure after the age of 18. Cases were collected from a big neurological clinic in Babylon governorate, Iraq. The period of study was extended from September 2007 to September 2010. The consent of all patients was taken and the study was done in accordance to guidelines of declaration of Helsinki.

Patients who had early or immediate seizure after suffering recent trauma and also a small number of patients with hypoglycemia were excluded. Each patient has at least two seizure attacks in his/her history. Data about the present illness, family, personal, and surgical history were recorded. Detailed physical and neurological examination for each patient was done. EEG, Computed tomography (CT), magnetic resonance image (MRI) were done for all the patients. MRI abnormalities were classified as generalized like brain edema, brain atrophy or localized like , brain tumors, infarction, atrophy or granuloma. Ancillary investigations like: cerebrospinal fluid (CSF), chest X-ray, complete blood picture, erythrocyte sedimentation rate, liver function tests, blood urea, blood sugar, serum lipid and abdominal ultra sound were done for selected patients. Treatment with anti epileptic drugs and response to it were observed and evaluated every month. Patients who are free from seizures on anti epileptic drugs (AED) are regarded good responders while those who are still having the attacks are regarded poor responders. EEG findings were classified as abnormal when there is clear epileptiform wave, slowing (focal or diffuse), phase reversal, change in the amplitude and clear asymmetry, otherwise it is regarded normal.

Seizures were classified according to the ILAE'S recommendation (2008), the etiology of epilepsy for each patient were classified as structural (brain tumor, CVD, post traumatic, inflammatory, degenerative), metabolic and unknown. Genetic causes were included within the group of unknown causes because of limited facilities. Comparison between different clinical and paraclinical results was done. Statistical analysis was done by SSPS software version 11. P value < 0.05 considered as significant level.

**RESULTS:**

A total of 102 patients met the criteria. The mean age of patients was 39.7 years with minimum of 18 and maximum of 75 years. 32(31.3%) were in the range of 18-29, 26(25.5%) in the range of 30-39, 18(17.6%) in the range of 40-49, 16(15.7%) in the range of 50-59, and 10(9.8%) were in the range of 60 and over. There were 63 (61.8%) male and 39 (38.2%) female (table 1).

According to medical history, examination, neuroimages and other ancillary investigation we found brain tumors in 24(23.5%) of cases, CVD in 23(22.5%), of those with CVD, 15(65.2%) had ischemic cerebral infarction, 5(21.7%) arteriovenous malformation (AVM) and only 3(13%) had hemorrhagic stroke (Table 3). Post traumatic cases were found in 13(12.7%) of cases. Inflammatory or infectious lesions, degenerative disorders and metabolic derangement were found in 9(8.8%), 4(3.9%), 4(3.9%) respectively. In 25(24.5%) I couldn't find a clear cause of seizure attacks (table 2). CVD cases were growing by each decade, but the tumor as an etiology of AOE had a peak value around

30-39 years and then its frequency decline, while the post traumatic cases, the large number were around 25-29 years (table 2).

Regarding intracranial neoplasm, the primary tumors were found in 20(83.3%), secondary metastatic tumors in 4(16.7%) of cases (table 4).

Regarding the inflammatory and infectious causes of AOE; granuloma was the most frequent cause. It was recorded in 5 patients (4.9%) of cases (table 9).

Seizures classification showed generalized tonic-clonic seizure in 47(46%) of cases, focal without impairment of consciousness (FWOIC) in 7(6.9%), focal with impairment of consciousness (FWIC) in 13(12.7%) and focal evolving to bilateral convulsive seizure (FETBS) in 35(34.3%). Other details are present in (table 6). Focal seizure was more frequent in cases secondary to CVD when compared to brain tumor cases. Of 23 patients with AOE due to CVD; 12(52.17%) had focal seizure, but in the group of seizure due to brain tumors only 8 out of 24 (33.3%) had focal seizures (P value < 0.02). EEG was positive in 55 (57.3%) of cases and within normal limits in 41(42.7%) of cases. The EEG findings are summarized in (table 6).

The MRI results were abnormal in (63.8%) of cases. More detailed are found in (table 7). Table 8 shows that 67(65.7%) of cases with AOE are well controlled by a single antiepileptic drug. The best

therapeutic responses were in patient who has CVD, inflammatory, or unknown causes. The poor controlled groups were in patients who had trauma, brain tumors or degenerative disorders.

MRI showed abnormalities in 65(63.8%) of cases, while EEG was positive in only 55 patients out of 96 (57.2%). So MRI abnormalities are more frequent than EEG abnormalities in AOE ( $P<0.05$ ) (Table 10)

### DISCUSSION:

Epilepsy is a symptom of numerous disorders, but in the majority of sufferers the cause remains unclear despite careful history taking examination and investigation<sup>(11)</sup>. The age of onset of epilepsy can give a clue to the causation. Causes of epilepsy after the age of 18 are so variable in both frequency and types.

This great variability depends on many factors which could be environmental, genetic in addition to the level of living. Brain tumors, either primary or secondary, account for 5-20% of cases of seizures occurring for the first time in adult<sup>(10, 12)</sup>. Seizure is the first symptom in 30% of brain tumors. In adult, a first seizure, particularly if focal should be evaluated by MRI for an occult brain tumor.

A study of 221 patients with AOE: from the university clinic of neurology, Hvidovre hospital. Copenhagen, Denmark, found that brain tumors were the cause in 16% of the cases<sup>(1)</sup>. Another study in Saudi Arabia found that brain tumors account for 20% of cases<sup>(13)</sup>. This study showed that brain tumors are the most common etiology of AOE in our country. This high percent may be explained partially by poverty, pollution and the burden of many wars sustained by the country.

The second important cause of AOE in this study was CVD. Epilepsy in adulthood constitute the following percent in many previous studies (7.5%), (14%), (18%), (19.3%), (20%) in Scandinavia, Denmark, Brazil, again Brazil, Saudi Arabia respectively<sup>(14, 1, 2, 15, 13)</sup>. This study showed that vascular causes of AOE is nearly similar to or little higher than that of the developing countries but it is much higher than that of the developed countries. A cerebrovascular basis for the AOE is supported by observation that seizure is more common in the presence of conventional risk factors for CVD such as hypertension, even without clinically overt stroke<sup>(16, 17)</sup>. Furthermore, altered cortical hemodynamic and / or metabolic parameters have been observed after subcortical stroke, and silent brain infarction have been observed<sup>(18, 19)</sup>. The

association between AOE and occult CVD is of crucial significance because such seizure could alert the physician to the like hood of elevated stroke risk, and prompt consideration of treatment of vascular risk factors in patient where this opportunity may otherwise not present itself<sup>(20)</sup>. The presence of an epileptiform discharge on EEG examination which occurs in 66.7% of cases of post stroke seizure is an important predictor for ongoing or recurrent seizure<sup>(21)</sup>. In addition, epileptiform discharges are important for early recognition of status epileptic's risk<sup>(22, 23)</sup>. Post stroke seizure is harmful and requires treatment with anti epileptic drugs<sup>(7)</sup>.

Post traumatic epilepsy is a well known fact that has been investigated thoroughly but as a cause of AOE, there are only few reports regarding this issue and these reports mentioned that trauma could be a major cause of AOE in some countries and a minor cause in other places<sup>(15, 24)</sup>. These variations apparently depend on the traffic facilities and the traffic laws and their strict application.

BA Yagub et al, in his study of 56 patients with epilepsy after the age of 20 in Saudi Arabia found that the incidence of cerebral granuloma was 7%<sup>(13)</sup>. Another study regarding inflammatory causes of epilepsy after 20 done by Medina in Mexico reported that neurocysticercosis or its sequale were diagnosed in 50% of cases. In the current study the infectious or inflammatory causes account for 8.8% of cases and 4.9% of them was due to granuloma. This result apparently indicates that granulomatous diseases are still endemic and common in our country and it represent a challenge for both neurologist and neurosurgeon. This problem must be suspected in every case of AOE who has fever, neck stiffness, recent contact with active tuberculosis and positive family history. The incidence of degenerative diseases was variable in many previous reports. One report mentioned that degenerative diseases were reported in 16% of cases<sup>(15)</sup>. Other report mentioned very low percent (1.6%)<sup>(14)</sup>. The low percent of degenerative disease in this study may reflect the low mean age of the sample that we studied, because this disorder is common in elderly patient above 60 years<sup>(26)</sup>.

We could not found any clear etiology in 25 patients (24.5%). This figure indicate that primary seizure may begin after age 18 and are not limited to adolescent or childhood, however close follow up of these seemingly unknown cases is essential. The previous reports about this issue are variable and the following percents are examples: 36%, 44%, and 50% 75.1%<sup>(1, 15, 26, and 14)</sup>. These variable

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figures may reflect the great variation in the causes of AOE from one place to another and it may be partially explained by the different designs and approaches by which these papers were done.

Almeida et al. showed that focal seizure, are the most frequent type of seizure in old age, although subsequent evolving to bilateral convulsive seizure often occur<sup>(27)</sup>. Our result regarding cases of seizure due to CVD was similar to the above results and it was 52% of cases, but in case of brain tumors it was registered in only 33% of them. Other reports about types of seizure in different types of causes of AOE were so variable.

Routine EEG was positive in 57.3% of cases and this result is in agreement with many previous reports<sup>(1,13,15)</sup>. MRI was conclusive in 63.8% of cases, this result indicate that MRI is the investigation of choice in AOE. This high yield of MRI in this study is apparently due to high percent of CVD, brain tumors, inflammatory and post traumatic cases in comparison to other studies where degenerative, alcohol withdrawal and unknown cases are the most frequent causes and obviously the last causes are usually not detected by this investigation.

Lastly therapeutic responses of most patients with CVD, inflammatory and the group with unknown cases was very good, but the control of epilepsy in

patients with brain tumors and post traumatic was poor and this result is a well known fact.

### CONCLUSION:

Brain tumors, CVD, post traumatic and inflammatory diseases are the four major causes of AOE in Iraq. Ischemic stroke is the most common cause of post stroke seizure and partial seizure is the most common type. Primary tumors form the highest percent of intracranial neoplasm usually between 30-39 years of age. The post traumatic epilepsy which constitutes the third major cause of epilepsy after the age of 18 has the largest number of cases between 20-29 years. Lastly granuloma is not uncommon in our country and it represents a challenge to the treating neurologist or neurosurgeon. The most common type of seizure among different group of etiologies is focal. Routine EEG was positive in more than half of cases and the common abnormalities are, sharp or spike with focal slowing and / or diffuses slowing. MRI is the investigation of choice in AOE and it was positive in approximately two third of cases. Most of the patient in this study showed good control of seizure with monotherapy. My recommendation is to deal carefully with each case of AOE, and in addition to proper history, physical and neurological examination, each patient must get, EEG, MRI and other ancillary investigation to exclude structural or metabolic causes of epilepsy which are common after the age of 18.

**Table 1: Age of sex distribution**

Age of onset	No. of Patients		Total (%)
	Male	Female	
≤ 29	16	16	32 (31.3)
30-39	18	8	26 (25.2)
40-49	12	6	18 (17.6)
50-59	12	4	16 (15.7)
≥ 60	5	5	10 (9.8)
Total (%)	63(61.8)	39(38.2)	102(100.0)

**Table 2: Causes of epilepsy According to age**

Age of onset	Brain Tumors	CVD	Post Traumatic	Inflammatory or infections Lesion	Degenerative Disorder	Metabolic Disorder	unknown	Total
≤ 29	6	4	6	2	2	1	8	29(28.4)
30-39	8	4	4	3	1	1	6	27(26.5)
40-49	4	3	2	2	-	1	5	17(16.7)
50-59	4	6	1	1	-	-	3	15(14.7)
≤ 60	2	6	-	1	1	1	3	14(13.7)
Total (%)	24 (23.5)	23 (22.5)	13 (12.5)	9 (8.8)	4 (3.9)	4 (3.9)	25 (24.5)	102 (100)

**Table 3: Cerebrovascular causes and age distribution**

	≤ 29	30-39	40-49	50-59	≥ 60	Total(%)
Cerebral ischemia	2	1	2	5	5	15(65.2)
AVM	2	2	1	-	-	5(21.7)
Hemorrhagic lesion	-	1	-	1	1	3(13%)

**Table 4: No. of patients according to the types of intracranial neoplasm**

Types of Tumors	No. of the patients
Primary Brain tumor	20
Astrocytoma	8
Oligodendroglioma	4
Glioblastoma Multiforme	4
Meningioma	4
Metastatic brain Tumor	4
Small cell carcinoma of the lung	2
Non Hodgkin's lymphoma	2

**Table 5: Distribution of causes and type of Seizure**

Causes	No. of patient	Primary Generalized	FWOIC	FWIC	FETBS
Brain Tumor	24	16	2	2	4
CVD	23	11	4	3	5
Post. Traumatic	13	8	-	1	4
Inflammatory	9	2	1	1	5
Degenerative	4	-	-	1	3
Metabolic	4	2	-	-	2
Unknown	25	8	-	5	12
Total (%)	102(100)	47(46)	7(6.9)	13(12.7)	35(34.3)

**Table 6: EEG Findings**

Causes	No. of patient	Abnormal	Normal
Brain Tumor	24/24	9	15
CVD	20/23	12	8
Post. Traumatic	13/13	10	3
Inflammatory	6/9	2	4
Degenerative	4/4	3	1
Metabolic	4/4	2	2
Unknown	25/25	17	8
Total (%)	96(100)	55 (57.3)	41(42.7)

**Table 7: MRI Findings**

Causes	No. of patient	Localized abnormality	Diffuse Abnormality	Normal
Brain Tumor	24	24	-	-
CVD	23	23	-	-
Post. Traumatic	13	7	-	6
Inflammatory	9	6	1	2
Degenerative	4	2	2	-
Metabolic	4	-	-	4
Unknown	25	-	-	25
Total (%)	102(100)	62(60.7)	3(2.9)	37(36.3)

**Table 8: Therapeutic responses to AED in different causes**

Causes	No. of patient	Good response	Poor Response	Dead
Brain Tumor	24	8	8	8
CVD	23	22	-	1
Post. Traumatic	13	6	7	-
Inflammatory	9	7	1	1
Degenerative	4	2	2	-
Metabolic	4	2	-	2
Unknown	25	20	-	5
Total (%)	102	67(65.7)	18(17.6)	17(16.7)

**Table 9: Types of inflammatory and infections causes**

Causes	No. of patient (%)
Granuloma	5 (4.9)
Cysticercosis	2 (2)
Encephalitis	1 (1)
Abscess	1(1)
Total	9 (8.8)

**Table 10 : EEG versus MRI yield in this study**

Test	Positive	Negative	No. of patient Examined
EEG	55	41	96
MRI	75	37	102

P value <0.05

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