Epilepsy at a University Hospital in Amman, Jordan

Yacoub G. Bahou, *MD, CES.*

ABSTRACT

Objectives: To study the clinical, EEG, neuroimaging, treatment results and outcome in Jordanian patients observed in a tertiary care referral center and compare the findings with those from Western and Middle/Far Eastern literature.

Methods: The case notes of 200 patients with epilepsy examined in an adult neurology clinic at Jordan University Hospital, Amman, Jordan, between January 2000 and December 2002 were reviewed. The findings of the EEG records and CT or MRI of the brain were registered. Seizures were classified according to the International League Against Epilepsy into generalized and partial seizures. The results of the treatment with antiepileptic drugs (AEDs) as well as the outcome were assessed.

Results: Among the 200 patients reviewed, 119 were female and 81 were male, with a mean age of onset of 24.6 years, the majority (85%) were below 39 years. The main seizure types were generalized in 128 (64%) patients (92 patients with tonic clonic (TC) seizures) and partial in 72 patients. Interictal EEG was abnormal in 69% of the patients. Neuroimaging showed brain lesions in 33.5% of the patients with a higher yield in partial (56%) than in TC seizures (30%). Sodium valproate and carbamazepine were the most frequently and efficiently used AEDs for generalized and partial seizures. After a 3 year follow-up, 76% were fully controlled with AEDs, outcome being better in generalized than partial seizures (worst in complex partial seizures).

Conclusion: Compared to the previous population on hospital based reports from Western and Middle/Far Eastern literature, our study showed a higher proportion of females and generalized seizures and a relatively better outcome with relatively similar early age of onset, yield of investigations and treatment modalities.

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Epilepsy is the most common serious neurological disorder and one of the world's most prevalent noncommunicable diseases. Over four-fifths of the 50 million people with epilepsy are thought to be in developing countries. Approximately 90% of people with epilepsy in developing countries are not receiving appropriate treatment.[1] The annual incidence of epileptic seizures ranges from 20-70 per 100,000 and the point prevalence is 0.4-0.8%.[2,3] Due to the high frequency and importance of this disorder in developing countries, this study was carried out in 200 Jordanian patients with epilepsy aiming to assess: 1. The age and gender distribution. 2. Seizure types and their relationship with age of onset. 3. Interictal EEG and neuroimaging findings. 4. Treatment and 5. Outcome.

The case notes of 200 consecutive patients with epilepsy examined in an adult neurology clinic at Jordan University Hospital (JUH), Amman, Jordan, over a 3 year period were reviewed. Results are compared with studies from Western and Middle/Far Eastern literature.

From the Department of Internal Medicine, Neurology Section, Jordan University Hospital, Amman, *Jordan.*

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Address correspondence and reprint request to: Dr. Yacoub G. Bahou, Department of Internal Medicine, PO Box 13046, Amman 11942, *Jordan*. Tel. +962 (6) 5353444. Fax. +962 (6) 5353388. E-mail: Jacobbahou419@hotmail.com

Table 1 - Age and gender distribution.

Age of onset (years)	Gender		Total
	Males	Females	
0-9	14	14	**28**
10-19	29	47	**76**
20-29	16	23	**39**
30-39	12	15	**27**
40-49	2	3	**5**
50-59	5	11	**16**
60-69	1	4	**5**
70-79	2	2	**4**
Total	**81**	**119**	**200**

Table 2 - Seizure types* according to age of onset.

Age range (years)	Generalized (N=128)				Partial † (N=72)	
	Tonic clonic	Juvenile myoclonic epilepsy	Absence	Atonic	Simple	Complex
0-9	11	-	2	-	7	**8**
10-19	27	25	6	-	7	**11**
20-29	23	-	2	-	4	**10**
30-39	15	-	-	-	4	**8**
> 40	16	-	-	1	9	**4**
Total	**92**	**25**	**10**	**1**	**31**	**41**

*According to the International League Against Epilepsy,
† - with or without secondary generalization.

Methods. The case notes of 200 patients with epilepsy observed in an adult neurology clinic at JUH between January 2000 to December 2002 were reviewed, some of them being transferred from the pediatric neurology clinic after reaching the age of 14 years. Jordan University Hospital is a tertiary care referral center with 530 beds, serving a considerable proportion of the Jordanian population. All patients had a detailed clinical history and neurological examination, initial blood tests (complete blood count, kidney and liver function tests) as well as standard EEG records using a 16 channel electroencephalograph (Model 9200k, Nihon Kohden Corporation, Tokyo, Japan). Video EEG using a Nicolet machine (Model BMSI 5000, USA) was carried out when clinically indicated or prior to epilepsy surgery.

All records were reported by the same neurophysiologist to minimize interobserver variability. Seizures were classified according to the International League Against Epilepsy[4] into generalized seizures [tonic clonic (TC), juvenile myoclonic epilepsy (JME), absence and atonic], partial seizures [simple partial epilepsy (SPE) or complex partial epilepsy (CPE)] and partial seizures with secondary generalization. All patients had CT scanning and the majority had MRI of the brain. Classical antiepileptic drugs (AEDs) such as carbamazepine (CBZ), sodium valproate (VAL), phenytoin (PHE), phenobarbital (PB) and clonazepam (CZ) were used as initial treatment while new AEDs such as topiramate (TPX), lamotrigine (LTG) and gabapentin (GB) were used as add on. Oxcarbazepine, levetiracetam, zonisamide and tiagabine were not utilized due to unavailability of the drug at JUH. Outcome was defined as full or partial control with AEDs or refractory epilepsy.

Results. Out of 200 patients, 119 were female and 81 were male (female to male ratio 1.5:1), mean age of onset was 24.6 years (range 2 months to 79 years). The age and gender distribution is shown in **Table 1** which indicates that the majority (170/200 or 85%) were below 39 years, the highest incidence (76/200 or 38%) being in adolescence (age range 10-19 years). **Table 2** shows seizure types according to age of onset. Out of 200 patients 128 had generalized epilepsy (TC 92, JME 25, petit mal absence 10, atonic 1) and 72 patients had partial epilepsy with or without secondary generalization (41 CPE and 31 SPE). Out of 92 patients with TC seizures, 54 were considered idiopathic either due to a positive family history in 10 patients or normal neuroimaging associated with generalized epileptiform discharges on EEG. The remaining 38 patients with TC seizures were either cryptogenic (namely, with epileptic focus but normal neuroimaging) or symptomatic (EEG focus and brain lesion). Thus, 89 out of 128 patients (70%) with generalized epilepsy were idiopathic, TC being the most common (54/89) followed by JME (25/89) and petit mal absence (10/89). In JME (n=25), myoclonus alone was noted in 5 patients, myoclonus with TC seizures in 17, myoclonus with absence in one and combination of all in 2. The mean age of onset in JME was 16 years (range 8-19 years) and majority (22/25 or 90%) were females. There was a delay in diagnosis of JME in 10 patients after a mean of 4.5 years (range 2-6 years).

Table 3 - Interictal electroencephalogram findings.

Result	Generalized				Partial		Total
	Tonic clonic n=92	Juvenile myoclonic epilepsy n=25	Absence n=10	Atonic n=1	Simple n=31	Complex n=41	
Normal	42	5	-	-	8	7	**62**
Abnormal							
Generalized Discharges	31	15	10	1	-	-	**57**
Focal Discharges	19	5	-	-	23	34	**81**
Total abnormal records	**50**	**20**	**10**	**1**	**23**	**34**	**138**

Table 4 - Findings on CT and MRI of the brain.

Result	Generalized tonic clonic seizures (n = 92)	Focal Seizures		Others*	Total
		Simple (n=31)	Complex (n=41)		
Normal	65	10	22	36	**133**
Stroke	13	5	4		**22**
Head injury	1	6	1		**8**
CNS tumor	4	4	5		**13**
CNS infection	1	5	-		**6**
Mesial temporal sclerosis	-	-	7		**7**
CNS vasculitis	2	1	1		**4**
Cortical atrophy	5	-	-		**5**
Multiple sclerosis	1	-	-		**1**
Cortical dysplasia	-	-	1		**1**

CNS - central nervous system, * - JME + absence + atonic
JME - Juvenile myoclonic epilepsy

Table 3 shows interictal EEG findings with abnormalities noted in 69% (138/200) of patients. Out of 128 patients with generalized epilepsies, 81 (63%) had generalized epileptiform discharges. Fifty-seven out of 72 (80%) with partial seizures had focal discharges. Twenty percent (5/25) of the patients with JME had focal epileptiform discharges.

Table 4 shows CT/MRI brain findings which were abnormal in 33.5% (67/200) of patients. Brain lesions were found in 56% (40/72) of patients with partial seizures and 30% (27/92) of those with TC seizures. Among the 13 central nervous system (CNS) tumors, gliomas were noted in 9 patients (one with neurofibromatosis), arachnoid cyst in 3 and brain metastases from lung cancer in one. Among the 6 patients with CNS infection, one had tuberculoma, one with brain abscess, one with hydatid cyst, one with herpes encephalitis and 2 with bacterial meningitides.

Regarding treatment and outcome, after a 3-year follow-up, 153 out of 200 patients were controlled with AEDs and are still on treatment, 104 with monotherapy and 49 with polytherapy. Full control was achieved in 109/128 (81%) of patients with generalized epilepsy and 44/72 (60%) of partial epilepsies. Out of 54 patients with idiopathic TC seizures, full control was achieved in 51 (94%),

using polytherapy in 7 and monotherapy in 44 patients (VAL in 17, CBZ 16, PHE 9 and LTG 2). Full control was attained in 25 out of 38 patients (69%) with cryptogenic or symptomatic TC seizures, 18 with monotherapy (CBZ 13, PHE 3 and VAL 2) and 7 with polytherapy. All our JME patients (n=25) were seizure-free with the treatment. Sodium valproate was efficiently used in 9 patients as initial treatment, 10 patients were initially started on CBZ due to TC seizures at onset and focal discharges on EEG but were later shifted efficiently to VAL when myoclonus appeared, 5 others were controlled with polytherapy (VAL+TPX+LTG) and one with CZ. Thus, 19 out of 25 JME patients, as well as all patients with petit mal absence, were controlled with VAL. The patient with atonic seizures improved on polytherapy.

Out of 72 patients with partial seizures, monotherapy was used in 20 and polytherapy in 52. The most frequently used AED was CBZ in 62 occasions followed by VAL 23, LTG 21, PHE 16, TPX 13, CZ 13, PB 10 and GB on 8 occasions. Despite polytherapy, 28 out of 72 patients (40%) were still uncontrolled, among them 19/41 (48%) with CPE and 9/31 (29%) with SPE, thus, showing a poorer outcome in the former. Seven patients with CPE were refractory and thus, referred for epilepsy surgery.

Discussion. Several points emerge from this retrospective study of 200 cases of epilepsy observed at JUH over a 3 year period. With respect to age of onset, 85% of our patients were below the age of 39 years, which is in agreement with other studies[5-8] where 50-81% of patients were below the age of 30 years. The mean age of onset (24.6 years) of our patients was similar to that found by Abduljabbar et al[5] but higher than that reported by others.[7,9] This might be explained by the fact that our patients were observed in an adult neurology clinic where almost 50% had onset of epilepsy above the age 20 years. Strikingly, 74 out of 200 (37%) of our patients had onset in adolescence, which is double the percentage reported by Pascual-Pascual.[10]

Concerning gender distribution, there was a predominance of females in our study (female to male ratio 1.5:1) which is in contradiction with other series[3-7,11] where males were more frequent (male to female ratios ranging from 1.5-2). With regard to seizure types, 68% of our patients had generalized seizures and 32% partial seizures with or without secondary generalization. This is in contrast to the findings of Ismail et al[11] (partial 67%, generalized 32%), Oller,[12] Hart et al[13] and Cockerell et al[14] based their studies on the newly diagnosed epileptic seizures (52% partial, 39% generalized). Among 30 patients above 40 years of age, generalized seizures (n=17) were more frequent than partial ones (n=13). This disagrees with Adachi et al[15] who reported that 70% of his 116 patients who are above the age of 50 years had partial epilepsy and Faught[16] who concluded that the majority of seizures in people above 60 years are partial mainly CPE. The predominance of generalized seizures in our patient cohort is explained by the fact that it included a significant proportion of seizures starting in childhood and adolescence (52% below the age of 19 years). Among generalized epilepsies TC seizures were the most common (92/128 or 72%) which is in accordance with other studies.[5,7,9]

Among idiopathic generalized epilepsies (n=89), TC seizures were also the most common (54/89 or 60%) followed by JME (25/89 or 28%). This contrasts with the study of Murthy et al[17] where among 2531 patients, JME was the most common form of idiopathic generalized epilepsy representing 4.9% of total study population. However, this figure of 28% approaches the 25% found by Montalenti et al.[18]

Among our 200 patients, JME accounted for 12.5% (25/200) which is a much higher prevalence rate compared to others,[17-21] where reported rates ranged from 5.7-8.3%.

The mean age of our JME patients was 16 years (range 8-28 years) which resembles other series[19,22-25] where mean ages ranged from 13.37-14.5 years. In accordance with other reports[24,26,27] there was a predominance of females in our JME patients (22 females, 3 males, ratio 7:1) yet our female to male ratio is much higher than that found by others[26,27] where it ranged from 1:1-2.9:1. Interictal EEG was abnormal in 138 out of 200 patients (67%) which agrees with Ismail et al[11] with 61.6% and King et al[28] with 68%. Surprisingly, despite that 52% of our patients had an early onset of epilepsy before the age of 19 years, yet focal epileptiform discharges represented 60% (81/138) of EEG abnormalities compared to 40% (57/138) generalized discharges. This concurs with Ismail et al[11] study of newly diagnosed seizures in adults where partial epileptiform discharges were seen in 48.9%, generalized discharges in 24.4% and non epileptiform abnormalities in 26.7%. Conspicuously, generalized spike or polyspike wave complexes were found in 80% (20/25) of our JME patients which agrees with other studies[19,20,24] where generalized discharges were noted in 79-96%.

Surprisingly, 20% of our JME patients had focal epileptiform discharges, similar to other reports.[18-20,27,29] There was a mean delay in diagnosis of 4.5 years in 10 out of 25 of our JME patients which was also noted by others[19-22,24,26,27,29,30] where mean delays ranged from 5.26-14.5 years. Montalenti et al[18] remarked that JME is widely under diagnosed and that at referral only 31.7% are

correctly diagnosed. Lancman et al[29] noticed a longer delay in diagnosis of 9.5 years in his JME patients with EEG asymmetries than in those without asymmetries (7.5 years). Panayiotopoulos et al[30] concluded that among 70 of his JME patients, 66 (91.4%) were not diagnosed in the epilepsy clinic. This delay in diagnosis is explained by the following: 1. Initial presentation with TC seizures. 2. Lack of reporting of myoclonic jerks by the patient or their families and 3. Unilateral myoclonic jerks or focal EEG discharges leading to a wrong diagnosis of partial epilepsy and thus, inappropriate initial AED.

Abnormalities seen through CT or MRI of the brain were found in 33.5% (67/200) of our patients which is similar to that noted by Ismail et al[11] in adults (29/73 or 39.7%) and by Aziz et al[9] who concluded that a putative cause for epilepsy was found in 38.4% of patients in Pakistan and 35.7% in Turkey. In our patients, brain lesions were more likely to be found in partial (56%) than in generalized epilepsies (30%). This is in agreement with Abduljabbar et al[5] who confirmed the association of partial epilepsy with clinical and CT abnormalities. Murthy et al[17] also remarked that single CT enhancing lesion and focal cerebral calcification accounted for 22% of the etiologic factors for localization which are related to epilepsies, thus, emphasizing the need for neuroimaging in patients with localization-related epilepsies with unremarkable clinical findings before classification in the cryptogenic category.

Concerning treatment and outcome, 76% of our patients were fully controlled with AEDs which is better than the other studies[7,31] where full control was achieved in 68% for the treatment and 48.8% for the outcome. In our patients, full control was better in generalized (81%) than partial epilepsies (60%). Among these patients with partial seizures, 71% of SPE and 52% of CPE were seizure free on AEDs. These results are better than what was found by Tanaka et al[31] with 39.4% for SPE and 40% for CPE but they agree with Ojemann[32] who concluded that AEDs control only half the patients with complex partial seizures. The most frequently and efficiently used AED in our 54 patients with idiopathic TC seizures was VAL or CBZ and in partial seizures CBZ. This is in full accordance with other reports.[33-35] Valproate as monotherapy was efficient in the majority (19/25) of our JME patients, which is similar to all other reports.[20,24,25,34,36] Because of misdiagnosis, 10 of our JME patients were initially started on CBZ but later shifted to VAL. This was also found by Atakli et al[20] where 52.6% (40/72) of their patients received AEDs other than VAL at initial interview and Grunewald et al[21] where 7 out of 15 patients received inappropriate AEDs. All our JME patients were seizure free with the treatment which is better than other series[20,24,25] where full control was achieved in 85.5-92.23%.

Among our 41 patients with complex partial seizures 19 (48%) were still uncontrolled despite polytherapy using old and new AEDs, thus, indicating the worst outcome in this seizure type, and among these 7 were refractory and referred for epilepsy surgery. This agrees with Ojemann et al[32] who concluded that patients with temporal lobe epilepsy refractory to drugs should be evaluated for resective surgery.

In conclusion, compared with other studies, ours demonstrates a similar high proportion of early age of onset but different gender distribution with female preponderance, a higher proportion of generalized epilepsies (mainly TC and JME), a similar sensitivity of EEG and neuroimaging particularly in partial seizures, a comparable efficiency of VAL in generalized and CBZ in partial seizures and a better outcome in generalized than partial epilepsy, the worst being in complex partial seizures.

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