Original Article

Adult onset idiopathic generalized epilepsy: A hospital-based study

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ABSTRACT

Objective: To find the occurrence of adult onset idiopathic generalized epilepsy (AOIGE) in patients attending the neurology outpatient department of a tertiary care centre.

Methodology: A prospective observational study was conducted in the Neurology outpatient department of Civil Hospital, Karachi between January 2004 and December 2008. All patients with new onset generalized epilepsy at age >25 years and with no evidence of an epileptogenic focus on history, clinical examination, electrophysiology, radiology or laboratory investigations were included. A structured pro forma evaluating detailed history, neurological & other systemic examination, electrophysiological, radiological and laboratory investigations were used to rule out focal epilepsy. Results were analyzed using SPSS 15.

Results: A total of 426 patients were enrolled. On evaluation, majority (85.6 %) were diagnosed as cases of symptomatic epilepsy with various etiologies like stroke, intracranial mass lesion, post infectious or post traumatic states and other rarer causes. In the remaining 61 patients (14.3%) there was no evidence of an epileptogenic focus on seizure history, clinical examination or investigations and were labeled as cases of AOIGE. Most patients (60.6%) were males and mean age of onset of seizures was 35.7 years. Three seizure types; generalized tonic clonic, myoclonic and absences were identified.

Conclusion: It was concluded that although adult onset idiopathic generalized epilepsy is not a common occurrence, but it does exist. However, adult onset epilepsies must be thoroughly investigated to rule out symptomatic epilepsy which is commoner than idiopathic epilepsy in this age group.

KEY WORDS: Adult onset epilepsy, Idiopathic generalized epilepsy.

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INTRODUCTION

About one-third of all epilepsies are idiopathic.[1] The incidence of idiopathic generalized seizures declines from 15/100,000 at age <1 year to 10/100,000 cases at 14 years and remains so in adult life until 65 years when incidence may rise again.[2] By convention, adult onset epilepsy should be considered epilepsy beginning after age 20 years, or according to some after 25 years. New adult onset idiopathic and generalized seizures are considered a doubtful entity by many, and researchers have often questioned their occurrence.

Apparently for many, adult onset idiopathic generalized epilepsy (AOIGE) is localization related

epilepsy related to traumatic brain injury sustained in the recent past or may represent unrecognized childhood or adolescence epileptic symptoms. AOIGE is considered a *de novo* occurrence of absence, myoclonic, and tonic–clonic seizures, alone or in combination during adult life. In last few years, evidence supporting the occurrence AOIGE has significantly increased.[3,4]

METHODOLOGY

A prospective study was conducted at the neurology outpatient department, Civil Hospital Karachi between January 2004 and December 2008. All patients with history of two or more, new onset generalized seizures, at or after the age of 25 years were recruited. A structured pro forma was developed and applied on the study patients A comprehensive seizure description and related seizure history was obtained; eyewitness account being mandatory. This was followed by a detailed clinical examination. All patients indicating a possibility of an epileptogenic focus on seizure semiology (aura, automatism, focal motor symptoms) were excluded. Patients with evidence of even a single seizure before age 25 years; on history or through medical records were also excluded as were patients with history of developmental delay and/or evidence of focal neurologic deficits arising in childhood. Patients with a positive family history of epilepsy were not included to avoid the remotest possibility of study subjects having earlier onset seizures that may have gone unrecognized. All patients with obvious brain trauma, accidental or surgical, were not taken into account. (Table-I)

EEG was routinely performed on all patients using 16-channel paper recordings lasting for 20–30 min during wakefulness and/or sleep states, including hyperventilation and intermittent photic stimulation. Patients with any focus on EEG were excluded even when the clinical history was suggestive of generalized seizures.

All patients had an MRI brain which, due to its higher yield of diagnosis was preferred over CT scan. All patients with any structural deformity or suspicion of a structural change were not included.

Metabolic, serologic and hematologic profile was carried out in all patients and included complete blood picture, ESR, urea, creatinine, electrolytes, calcium, magnesium, LFTs, ANA, TSH, and urine examination. Patients with abnormal laboratory results were excluded considering the possibility of provoked seizures.

To rule out cardiac arrhythmias or syncope as a possible cause for falls or loss of consciousness in selected patients with history of palpitation or seemingly non-epileptic falls, cardiac consultations, ECG, Holter monitoring and tilt table testing were also undertaken.

The patients were sorted according to gender. Age at seizure onset was noted. Seizures were classified according to the 1981 International Classification of Epileptic Seizures. Frequency of these seizures was questioned in terms of the number per day, week, month or year. Patients were also asked about the provoking factors and postictal events.

Impact of seizures on work and routine activity in the study patients was also taken into account. Impact was measured as person easily performing routine activity (Category I) with no (Ia) or little (Ib) change in lifestyle, those compelled to work routinely due to their financial or other restraints (Category II), those compelled to work less due their seizures or change occupation (Category III), those totally disabled due to their seizures (Category IV) and those who could work but did not, due to fear or simply making seizures an excuse for not working (Category V).

RESULTS

During the four year study period 426 adult patients with history of new onset unprovoked seizures at or after 25years age were enrolled. On

Table-I: Inclusion & Exclusion Criteria.

Inclusion criteria
* All patients with new onset generalized epilepsy at age >25years.
Exclusion criteria
History
* Aura
* Focal onset or termination of seizures
* Medical record evidence of earlier seizures
* Family history of epilepsy
* Early developmental delay
* Trauma accidental or surgical
Examination
* Focal neurological deficits
Electrophysiology
* EEG: Focal seizure activity
* ECG: Cardiac arrhythmias
MRI
* Any structural abnormality
Laboratory
* Abnormal hematology
* Abnormal Biochemistry
* Abnormal Serology

Table-II: Causes of Adult Onset Symptomatic Epilepsy

Disorder	*Patients (n)*
Stroke	167
Brain Tumors	63
Post-Traumatic	24
Post-Infectious	93
Others	18
	365

evaluation, 365 patients (85.6%) were diagnosed to be having symptomatic epilepsy. Identified causes for symptomatic epileptic seizures are tabulated in Table-II. Patients with stroke included ischemic, haemorrhagic as well as vasculitic strokes. Others included patients who had doubtful demyelination on MRI (no=4), or no abnormal neurological investigations but had doubtful cardiac arrythmias, history of syncope, and uremia. Recurrent hypoglycemia in a patient with insulinoma was also found to be the cause of his provoked seizures.

However, 61 (14.3%) of the patients did not have any apparent cause for epileptogenesis on detailed evaluation and were labeled as cases of AOIGE. These patients formed our study group (n=61); majority being males (60.6%). Age at presentation of AOIGE patients ranged from 26 to 77 years with a mean age of 41.8years. Mean age at onset of seizures was 35.7 years; 23 (34.4%) patients presented in age group 25-35 years, 23 (37.7%) in 36-45 years age group, 7 (11.4%) in ages ranging from 46 to 55 years and 9 (14.7%) >55years age.

Among the seizure types majority (77.04%) had generalized tonic seizures (GTCS). Two had frequent absences with no automatism or any other focal features to suggest complex partial seizures, and occasional generalized seizures. Seven patients (11.4%) had myoclonic jerks along with generalized tonic clonic seizures and four (6.5%) reported isolated myoclonic seizures, making eleven (18.03%) patients with adult onset myoclonic epilepsy.

EEG was normal in 44 (72.2%); generalized seizure discharges pattern was seen in only 17 (27.8%). Three patients (4.9%) with generalized discharges had clinical myoclonic seizures during the recording and revealed concordant EEG changes. Absences were not recorded on EEG in any of our patients.

Identifiable triggers were present in only 13 (21.3%) patients. Lack of sleep was a trigger for all these people whilst two patients additionally reported severe stress or fatigue as provoking causes. The remaining 48 (78.7%) could not recall any triggers for their seizures. Seizure frequency ranged from one per year to nearly daily myoclonic seizures. GTCS were less frequent while myoclonic jerks and absences occurred more frequently.

Table-III: Comorbid Conditions.

Comorbid Condition	*No.*	*%*
Hypertension	12	19.6
Diabetes mellitus	6	9.8
Osteoarthritis	13	21.3
Asthma	2	3.2
Menstrual abnormalities	3	4.9
Fibroid uterus	1	1.6
Atopy	1	1.6
Psychiatric illness	13	21.3

Eighteen (29.5%) patients reported no post-ictal events. Among other 43 (70.4%) patients headache was the commonest post-ictal symptom reported, occurring in 21(34.4%) patients. Other less commonly reported symptoms included body aches, confusion, lethargy and tendency to fall asleep.

Thirty one (50.8%) study patients were already on AEDS when they first attended the study setting. One patient each reported going to homeopathic and ayuvedic physicians and 8 (13.1%) patients had visited their local spiritual healers. One third patients (33.3%) did not seek any help for seizure control before reporting to our OPD.

Interesting results were obtained while analyzing the impact of adult onset epilepsy on work and routine activities. Majority of our patients, n=35 (57.3%) reported no significant effect on work with no (n=16) or little (n=19) modification in their lifestyles. Lifestyle modifications included abstinence from driving, avoiding swimming alone, hiring help for house work etc. Six (9.8%) patients reported they were compelled to work in spite of seizures because they could not abandon their work or study due to one reason or other. Another group, comprising eight (13.8%) people reported that they could not work in their full capacity and their work output was compromised. Only 3 (4.9%) patients reported that they could not work at all due to their seizures. One patient, a tailor by profession, had frequent myoclonic jerks and other two with GTCS were taxi driver and truck driver respectively. The most interesting part was that 9 (14.7%) patients could work but did not with an excuse of their illness.

Systemic comorbidities were found in 38 (62.2%) patients, 12 (19.6%) having more than one coexisting

illnesses, while 23 (37.8%) were clinically healthy otherwise. These comorbid conditions are summarized in Table-III.

DISCUSSION

We identified 61 (14%) patients with AOIGE out of 426 patients with onset of seizures at e"25 years. In rest of the patients epilepsy was "symptomatic." Cutting et al reported similar figures (13.4%) amongst their 313 patients with onset of epilepsy after 18 years of age.[3] In contrast, Nicholson et al in his study of patients with idiopathic generalized epilepsy at all ages[4] identified only 9.7% with onset after 20 years age and it was reported in 28% by Carini et al.[5] Zarrelli et al[6] found that that the annual age-specific incidence of IGE in patients aged 25–34 years was 3.5 per 100,000. This clearly documented that like in other parts of the world, AOIGE does exists in our population.

Although epilepsy is considered equally prevalent amongst the two genders, men are slightly more affected than women and except for absence seizures all other types of seizures are slightly more common among men than women.[2] We found men to have adult onset epilepsy more commonly than women which was also observed by Nicholson A. et al[4] who compared clinical features of adult onset epilepsy with classical generalized epilepsy.

Comparing mean age at onset with other researchers we found that ours was the oldest mean age at seizure onset, that is, 35.7 years. This was despite the fact that our cut off age for patient inclusion was higher than in other similar studies In studies with cut off at 20 years,[4,5] reported mean onset age was 23.8 years[4] and 33years[5] with similar results (23.8 years) with cutoff age 18 years.[3] Although Loiseau and colleagues[7] searched for cases of IGE beginning after the age of 60 years and found none. However, our oldest patient to report AOIGE was 77 years whilst 09 patients were >55 years age.

Mainly three clinical subtypes were distinguished; generalized tonic clonic, myoclonic and absences. Majority of our patients had generalized tonic clonic seizures, a common observation shared by all those who looked into various aspects of adult onset epilepsy. This was followed by myoclonic seizures, isolated or in conjunction with tonic-clonic type. Gilliam et al[8] recently described adult myoclonic epilepsy as a distinct syndrome that occurs with no previous childhood or adolescent seizures. Absences occurred in only two patients who occasionally experienced GTCS too. Absences were brief blank spells with no focal features to suggest complex partial seizures and were not recorded on EEG even on augmentation by hyperventilation which is usually a feature seen in younger patients. Berkovic and Benbadis[9] like most others cast serious doubts on diagnosis of absences if EEG remains normal with hyperventilation. However, Oller[10] suggested that sudden onset and sudden termination of absence without postictal confusion allows one to distinguish absences from complex

Table-IV: Results at a glance.

- * Total no.: 61

Gender
- * M=37 (60.6%)
- * F=24 (39.3%)

Age at seizure onset
- * Age range: 25-77 years
- * Mean age at seizure onset: 35.5y
- * 25-35 years: 21(34.4%)
- * 36-45 years: 23(37.7%)
- * 46-55 years: 7(11.4%)
- * >55years: 9(14.7%)

Type of Seizures
- * GTCS: 47 (77.04%)
- * Absences: 2 (3.2%)
- * Myoclonus with GTCS: 7(11.4%)
- * Isolated myoclonic jerks: 11 (18.03%)

EEG
- * Normal: 44 (72.2%)
- * Abnormal: 17 (27.8%)

Identifiable Triggers
- * Present: 13 (21.3%)
- * Absent: 48 (78.6%)

Post-ictal Events
- * Yes: 18 (29.5%)
- * Commonest Symptom: Headache 21(34.4%)
- * No: 43 (70.4%)

Effect of Seizures on Work Output
- * No effect: 16 (26.2%)
- * Minimal effect: 19 (31.1%)
- * Compelled to work: 6 (9.8%)
- * Reduced efficiency: 8 (13.8%)
- * Could not work: 3 (4.9%)
- * Could work but did not: 9 (14.7%)

partial seizures. The rarity of adult onset absence epilepsy over the age of 25 years suggested that either this syndrome was exceedingly rare or under-recognized in all populations including ours.

The diagnosis of epilepsy is essentially a clinical one. In the majority of patients with clinical events, a normal EEG does not exclude epilepsy. EEG was positive in only 27.8% of all patients. Ajmone et al[11] reviewed 1,824 EEGs in 308 people with epilepsy. In 92 patients (30%), all the EEGs contained epileptiform discharges. Fifty-four patients (18%) never exhibited epileptiform discharges despite repeated EEGs over several months. Epileptiform discharges were found on some occasions, but not on others, in 162 patients (52%). Overall, epileptiform discharges were found in 55% of patients at the first examination. Like Suthida et al[12] we also did not find any differences in the morphological features of EEG, normal or abnormal, from those with younger onset epilepsy.

Seizure precipitants like sleep deprivation and stress were also reported by other authors[4,5] but reports on fatigue and physical activity are controversial. In Nakken's study which compared seizure precipitants in three twin registries, tiredness was the most common seizure precipitant, but physical activity was a precipitant in 6% of Norwegian population and only reported in 0.3% and 0.7% of Danish and American population respectively.[13]

Seizures can be a burden with a negative impact on quality of life, affecting activities of daily living, independence, work, and driving. In our study we have tried to assess an important aspect of burden of epilepsy that is, the social impact as perceived by the patient or family. On literature search we were unable to find a study reporting this aspect in patients with AOIGE.

CONCLUSION

We conclude that although adult onset idiopathic generalized epilepsy is not a common occurrence it does exist. However, this does not undermine the importance of detailed investigations required in all patients reporting a first ever seizure in adult age. Further research and follow up studies are needed in determining the burden of adult onset epilepsy, its response to various therapies, effectiveness of different drugs compared to classical epilepsy, and the natural course and prognosis.

REFERENCES

1. Gastaut H, Gastaut J, Goncalves E, Silva GE, Fernandez Sanchez GR. Relative frequency of different types of epilepsy: A study employing the classification of the International League Against Epilepsy. Epilepsia 1975;16:457–461.
2. Annegers JF. The Epidemiology of Epilepsy. In: The Treatment of Epilepsy. Lippencott Williams & Wilkins. Third Ed. 2001: 134.
3. Cutting S, Lauchheimer A, Barr W, Devinsky O. Adult-Onset Idiopathic Generalized Epilepsy: Clinical and Behavioral Features. Epilepsia 2001;42(11):1395–1398.
4. Nicolson A, Chadwick DW, Smith DF. A comparison of adult onset and ''classical'' idiopathic generalized epilepsy. J Neurol Neurosurg Psychiatry 2004;75:72–74.
5. Marini C, King MA, Archer JS, Newton MR, Berkovic SF. Idiopathic generalized epilepsy of adult onset: Clinical syndromes and genetics. J Neurol Neurosurg Psychiatry 2003;74:192–196.
6. Zarrelli MM, Beghi E, Rocca WA, SW. Allen Hauser Incidence of Epileptic Syndromes in Rochester, Minnesota: 1980-1984 Epilepsia I999;40(12):1708-1714.
7. Loiseau J, Crespel A, Picot MC, Duche B, Ayrivie N, Jallon P, et al. Idiopathic generalized epilepsy of late onset. Seizure 1998;7:485–487.
8. Gilliam F, Steinhoff BJ, Bittermann HJ, Kuzniecky R, Faught E, Abou-Khalil B. Adult myoclonic epilepsy: A distinct syndrome of idiopathic generalized epilepsy. Neurology 2000;55:1030–3.
9. Berkovic SF, Benbadis S. Absence seizures. In: The Treatment of Epilepsy. Lippencott Williams & Wilkins. Third Ed. 2001: 357.
10. Oller LF-V. Childhood absence epilepsy and juvenile absence epilepsy. In: Handbook of Clinical neurology. Vol 73(29). The Epilepsies, Part II. Elsevier Science B.V. 2000: 146.
11. Ajmone-Marsan CA, Zivin LS. Factors related to the occurrence of typical paroxysmal abnormalities in the EEG records of epileptic patients. Epilepsia 1970;11:361-81.
12. Suthida Yenjun, Harvey AS, Marini C, Newton MR, King MA, Berkovic SF. EEG in Adult-onset Idiopathic Generalized Epilepsy. Epilepsia 2003;44(2):252–256.
13. Nakken KO, Solaas MH, Kieldsen MJ, Friis ML, Pellock JM, Corey LA. Which seizure precipitating factors do people with epilepsy most frequently report? Epilepsy Behav 2005;6:85-89.