



# Two-tier System of Epilepsy Evaluation: A Useful Method for Developing Countries

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## Abstract

**Purpose :** To test the usefulness of a simplified and clinically oriented, the Epidemiological Classification (EC), in determination of seizure types and appropriate drug selection in epileptic patients at the primary care level.

**Methods :** The EC was applied to all epileptic patients over 5 years then compared with the currently recommended international classifications of seizures and epilepsy (ICES/ICEES).

**Results :** A total of 1176 patients were enrolled with 2:1 male preponderance and 88% had onset of disease below 30 years of age. Based on EC, 682 (58%) had partial, 333 (28.3%) had generalized and 161 (13.7%) had undetermined seizures semiology. When ICES was applied, seizure typing was same in 86.2%, 68.5% and 26.7% patients of partial, generalized and unclassified seizures respectively. About 87% patients in generalized and partial seizure semiology had no change in selected antiepileptic drug even after the ICES, but 53.6% patients in undetermined group had change in selected AED. Only, 146 patients (12.5%) found to have symptomatic cause for seizure(s) on applying the EC system. After utilizing the ICEES on 1030 patients (87.5%) of "unknown etiology" cases after the EC system, almost 86.5% patients could be classified to a definite etiological class.

**Conclusion :** The EC was found useful for determination of seizure type and appropriate AEDs selection at the primary care level. The ICES/ICEES works better at the tertiary care level. This "two-tier" system can be more effective for overall epilepsy management in developing countries with limited facilities. ©

## INTRODUCTION

The International League Against Epilepsy (ILAE) has developed guidelines for the classification of epileptic seizures and epileptic syndromes, termed as International classifications for epileptic seizure (ICES) and for epilepsies and epileptic syndrome (ICEES)<sup>1-3</sup> Doctors, usually neurologists in India, who have been trained in the field of epilepsy, can only utilize these classifications in their clinical practice. There are only 500 neurologists for the one billion people in India for about 8 million (70% in rural areas) epileptic patients.<sup>4,6</sup> Most of these patients almost always approach to nearby placed general practitioners (GPs), who are usually not trained to apply the ICES/ICEES. Secondly, the ICES/ICEES need support of lab investigations like Electroencephalography (EEG), which is usually not available at the primary care level. Thus, the ICEES system was criticized due to its complexity and a pressing need was felt for a more simplified, practical and clinical classification for the primary care level.<sup>7,8</sup> Few types of epilepsy remain

unrecognized and wrong antiepileptic is selected in patients of epilepsy without a proper classification of seizures at the primary level.<sup>9-13</sup>

In the search of a simpler classification system, we found another ILAE classification that was developed in 1993 for conducting epidemiological survey on epilepsy.<sup>14</sup> This was named the Epidemiological Classification (EC) and was proposed for only research purposes to overcome technical problems in field studies (Table 1). The striking points in this classification are; 1) it has semiology-based classification of seizures typing, 2) it presents a simple categorization of risk factors causing seizure(s), and 3) there is no need to study large number of epileptic syndromes for clinical application. Therefore, it has all property to use it for clinical practice at the primary care level. Unfortunately, the EC system was never utilized for diagnosis and treatment of epileptic patients at the primary care levels. Thus, we planned to use the EC system in epileptic patients and compare it with the ICES/ICEES system. We are presenting the utility of this EC system for classification of seizures and appropriate antiepileptic drug selection at the primary care level.

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Received : 19.6.2008; Revised : 18.8.2008;  
Accepted : 31.10.2008

## MATERIALS AND METHODS

**Table 1 : Showing short outline of the Epidemiological Classification (EC)<sup>14</sup>**

Classification of seizure	
2.1.	Generalized seizures – when clinical symptomatology provides no indication of an anatomic localization and no clinical evidence of focal onset. Three main subtypes were defined: Generalized convulsive seizure (GTCS) – With predominant tonic, clonic or tonic-clonic features. Generalized non-convulsive seizures – Absence seizures, myoclonic, tonic, atonic
2.2	Partial seizure – when there is evidence of a clinical partial onset (by aura or focal symptoms). Further divided into: Simple partial – ability to interact appropriately with the environment is maintained. Complex partial – impairment of consciousness, amnesia and/or confusion is there, during or after a partial onset seizure. Secondary GTCS – Generalized Tonic-Clonic seizure after focal onset or Aura.
2.3/2.4	Undetermined seizures – it is impossible to classify seizures owing to lack of adequate information or variable/mixed partial and generalized seizures.
Risk factors or etiology	
3.1	Symptomatic seizures or epilepsies – consequence of a known cerebral dysfunction
3.1.1	Acute symptomatic – seizures are in close temporal association (within 7 days) with an acute systemic, metabolic or toxic insult and with acute CNS insult (infection, stroke, cranial trauma, intracerebral hemorrhage, acute alcohol intoxication or withdrawal).
3.1.2	Remote Symptomatic – seizures in relation to a well-demonstrated antecedent condition called as remote symptomatic seizures or epilepsy (more than 7 days of cerebral insult).
3.2	Unknown etiology – no clear antecedent etiology can be detected.

All patients presenting with seizure(s) as a primary symptom were evaluated in a prospective, open-label study at the epilepsy clinic of the Himalayan Institute Hospital from January 2001 to December 2005. Patients having acute symptomatic seizures with obvious provoking factors like acute head injury, cerebro-vascular event, meningitis, encephalitis, metabolic-septic insults, etc. were not included in the study. All patients were evaluated in following manner;

Step 1 – Demographic profile and clinical variables, including age of onset of seizures, gender, duration of illness, family history of febrile seizures or epilepsy in first degree relatives, past history of febrile convulsions, history of perinatal trauma, past history of any neurological or psychiatric illness, past head injury (with at least 30 minutes loss of consciousness), any brain surgery in the past and reason for consultation (new case, poor control and relapse after discontinuing AEDs) were recorded.

Step 2 – Seizure type and risk factors for seizures were defined and classified according to the ILAE Epidemiological Classification (EC). Seizures were divided into generalized, partial, mixed and unclassified type, based on clinical semiology. Then etiology was defined as acute or remote symptomatic or unknown etiology based on clinical details.

Drug selection was also based on seizure semiology and for partial seizures phenytoin or carbamazepine/oxcarbazepine was given, while in generalized, mixed or undetermined seizures valproate or phenobarbitone was given as first choice. In case of a change in seizure typing or poor control of seizures during follow-up, antiepileptic was accordingly changed.

Step 3 – After applying the EC system and starting AEDs all patients with unknown etiology were subjected to investigations to apply the ICES/ICEES system. After 30 minute inter-ictal electroencephalography (EEG) recording, findings were classified into a) normal, b) generalized or focal epileptiform abnormalities, and c) non-epileptic abnormalities. Post-contrast computed tomography (CT) or magnetic resonance imaging (MRI) was carried out on all patients except those with generalized epileptiform discharges.

## RESULTS

A total of 1176 patients were enrolled during the study period. There was a 2:1 male preponderance. Median duration of illness was 3 years (range 2 days-41 years). Most of the patients (88%) had onset of disease below 30 years of age. A family history of epilepsy in first-degree relatives was present in 76 patients (6.5%); abnormal mental or neurological development in 88 patients (7.5%). Past history of febrile seizure was positive in 55 patients (4.8%). Only 490 patients (41.7%) registered as new onset of seizures while the rest of the patients (58.3%) had a history of using some kind of antiepileptic therapy before registering at our center. Median duration of follow-up was 15 months (range 0-62 months).

Distribution of various seizure type, based on clinical semiology according to the EC (partial, generalized, and undetermined) are given in Table 2. Based on semiology partial seizures were more common in 682 (58%) patients. In 161 (13.7%) patients, seizure semiology could not be determined due to inadequate information e.g. seizures during sleep, mentally retarded patients, unseen seizures or mixed partial and generalized semiology. When the ICES applied to these patients, determination of seizure type was correct in 86.2%, 68.5% and 26.7% of partial, generalized and undetermined seizures of the EC category, respectively. Even after the ICES, 63 (9.3%) of partial, 62 (18.6%) of generalized and 43 (26.7%) patients of undetermined seizure semiology remained unclassified. After combination of the EC and ICES, only 43 (3.7%) patients remained truly unclassified for seizure typing.

Among 327 (89.2%) patients of generalized and 136 (84.5%) with undetermined seizure semiology were prescribed valproate (VPA) while in 596 (87.4%) patients of partial seizure semiology were given carbamazepine (CBZ) or oxcarbazepine (OXC) as first AED. Most of the patients with generalized (87%) or partial semiology (86.2%) had no change in selected first antiepileptic drug even after the ICES, but 87 (54%) patients of undetermined group had

Table 2 : Showing comparison of seizure types on epidemiological (EC) and international (ICES) classification

Seizure semiology based on EC N (%)	Seizure type based on ICES (1981) Classification		
	Generalized N (%)	Partial N (%)	Unclassified N (%)
Generalized 333 (28.3%)	228 (68.5%)	43 (12.9%)	62 (18.6%)
Partial 682 (58%)	31 (4.5%)	588 (86.2%)	63 (9.3%)
Undetermined 161 (13.7%)	31 (19.3%)	87 (54%)	43 (26.7%)
Total	290 (24.7%)	718 (61%)	168 (14.3%)

EC – Epidemiological classification; ICES – International Classification of Epileptic Seizure

Table 3 : Effectiveness of the epidemiological classification for AED selection

Seizure semiology After the EC system Type (number)	No change in choice of 1 <sup>st</sup> AED after ICES N (%)	Change in first AED after ICES N (%)	Good seizure control on first AED in follow-up N (%)	No follow-up N (%)
Gen (333)	290 (87%)	43 (13%)	190 (57%)	38 (11.4%)
Partial (682)	588 (86.2%)	94 (13.8%)	389 (57.1%)	65 (9.5%)
Undetermined (161)	74 (46%)	87 (54%)	49 (20%)	11 (6.8%)

AED – Antiepileptic Drug; EC – Epidemiological Classification; ICES – International Classification of Epileptic Seizure

change in selected AED during follow-up (Table 3). Almost 57% patients in both partial and generalized semiology group had good seizure control on selected AED, while only 20% patients of undetermined semiology had good seizure control on first AED (Table 3).

Only 146 patients (12.5%) found to have some acute or remote symptomatic cause for seizure(s) on applying the EC system (Table 4). In acute symptomatic group, febrile seizures (11 (0.9%) patients) and in remote symptomatic, perinatal trauma (49 (4.2%) patients) and head injuries (43 (3.7%) patients) were the most common risk factors. After utilizing the ICEES on 1030 patients (87.5%) of “unknown etiology” cases after the EC system, almost 86.5% patients could be classified to a definite etiological class (Table 5). The most prominent groups with syndromic classification were in class 1.2 (22.5%), 2.1 (26.2%) and 4 (29.9%). Only 20.3% remained in the non-specific etiology group after the ICEES (ILAE class 1.3 (6.1%), 2.2/2.3 (0.7%) and 3 (13.5%).

## DISCUSSION

For the first time two international classification systems were used in combination for the improvement in epilepsy management at primary care levels. Our study had suggested that the EC system was useful for correctly classifying the seizure type and appropriate AED selection in large number of patients without investigation. This tool can be helpful for reasonably good initial treatment of seizures cases at remote areas. Most important limitation of the EC system was poor yield of the etiological diagnosis. On the other hand the ICES/ICEES system was better in classification of undetermined seizures type and etiologies at the centers with all facilities.

There are four basic steps in the evaluation of patients with epilepsy: 1) classification of epileptic seizures; 2) determination of the etiology causing seizure(s); 3) selection of appropriate antiepileptic drugs (AEDs) and 4)

Table 4 : Risk factors for seizures after the epidemiological classification

Risk factors	Number of patients (%)
Known etiology	146 (12.5)
3.1.1 (Acute symptomatic)	11 (0.9)
all excluded except Febrile convulsion	
3.1.2A (Static Remote)	
Old Perinatal trauma	49 (4.2)
Old head injury	43 (3.7)
Febrile encephalopathy in past	14 (1.2)
Old cerebro-vascular accident	15 (1.3)
Old cranial surgery	6 (0.5)
3.1.2B (Progressive Remote)	
Degenerative	8 (0.7)
3.2 (Unknown Etiology)	1030 (87.5)

Table 5 : Etiological class according to the international classification of epilepsies and epileptic syndromes (1989)

Type of epilepsy	Number of patients (%) (n=1030)
1 - Localization related epilepsies	306 (29.7)
1.1 - Idiopathic	11 (1.07)
1.2 - Symptomatic	232 (22.52)
1.3 - Cryptogenic	63 (6.12)
2. Generalized epilepsies and syndromes	277 (26.9)
2.1 - Idiopathic	270 (26.2)
2.2/2.3 - Symptomatic (probably symptomatic)	7 (0.68)
3.0. Epilepsies and syndrome undetermined whether focal or generalized	139 (13.5)
4.0. Situation related seizures	308 (29.9)

decision for discontinuation of AEDs after a certain period of seizure remission. Without having answers to the first two questions, one cannot proceed toward the next two steps. The general practitioners (GPs) and government medical officers are the backbone of the primary care system in many developing countries. A Study, evaluating referral

patterns of epileptic patients to the tertiary care hospitals, has shown that patients are poorly classified and managed at the primary care level.<sup>15</sup> A few other studies have been conducted on the performance of GPs in epilepsy care, but unfortunately, the issue of how GPs classify epilepsy has not been given due importance in these studies.<sup>16,17</sup> It is evident that despite decades after introduction of the international classification systems (ICES and ICEES), their utility in clinical practice at primary care level is disappointing.<sup>13</sup> About 60% of our patients were already seen and treated by primary care physician (mostly GPs) and none had used the ICEES terminology while referring the patients. It seems that the EC system can be better utilized for classification and treatment of large number of epileptic patients seen by primary doctors who cannot apply the ICEES.

An accurate classification of seizures type is essential before appropriate AEDs selection by the primary care physicians. Existing guidelines suggest that, out of four conventional AEDs, phenytoin sodium or carbamazepine is better for partial seizures and phenobarbitone or sodium valproate better for generalized or undetermined seizures.<sup>18</sup> A wrong classification of seizures types at the primary care level can result in wrong selection of AEDs in many patients. At the primary care level frequency of generalized seizures is overestimated in comparison to hospital study due to improper classification and non availability of investigation.<sup>19,20</sup> Evaluation of seizure type by clinical semiology seems to be more practical at the primary care level rather than the electro-clinical ICES system because of non-availability and high rate of normal finding in first EEG.<sup>21</sup> Lastly, we recommend that patients having undetermined seizures type by the EC system should be referred as early as possible to the tertiary care center to prevent wrong diagnosis and treatment.

It seems from our study that about 57% patients can be managed at the primary levels without any difficulty with the EC. Patients with partial or generalized seizures after the EC system who respond well to first AED can continue their medicine for appropriate duration (2 to 3 years) and then discontinuation of AED can be done according to the MRC guidelines.<sup>22</sup> But if seizures are poorly controlled or relapsing after AED discontinuation then evaluation at higher centers is essential, and this is another indication for the tertiary care referral. Thus, evaluation of seizure type and etiology with the ICES/ICEES system at the tertiary level will be required for limited number of patients. This will reduce the cost of epilepsy care and need of investigations in developing countries like India having limited specialty care centers. One limitation in our study is that it has been done at referral center not at primary care level. The further confirmation of our results needs a large multi-centric study that includes both the primary care and tertiary care physicians.

To summarize in developing countries with limited resources about half of patients with seizures can be classified and treated effectively at the primary care level with help of the EC system. Patients, those who are

unclassifiable, get seizure relapse after AED withdrawal or poorly controlled on drugs after application of the EC system, can be referred to the tertiary care level for application of the ICES/ICEES. The EC and ICEES systems are found to be complimentary to each other and can be used simultaneously at two different levels of health care in developing countries therefore named as "two-tier" system. The first tier (EC system) of this "two-tier" system can help a large number of patients seen at the primary care levels or small hospital/clinic settings by the doctors who cannot use the ICEES. The EC system is easy to understand by medical undergraduate and the primary care physicians. This system can give better results in epilepsy management at primary care level in comparison to current practice. The second tier (ICEES system) is useful for those patients who are either directly reaching a specialist in epilepsy care or those who have been referred to the tertiary level due to a doubt in diagnosis or poor control of seizures on AEDs.

## CONCLUSIONS

None of the existing classification systems by the ILAE is useful in isolation for day-to-day management of large numbers of epileptic patients. However, there is evidence from this study that combining the EC with the ICEES classification into a two-tier system of evaluation can be more effective, in management of large numbers of epileptic patients at primary care levels. The two-tier classification system of it will boost the confidence of the primary care physicians as they communicate with specialists at the tertiary care level.

Disclosure of Conflicts of Interest - None of the authors has any conflict of interest to disclose.

## Acknowledgements

We thank to Dr Vikas Agarwal Assistant Professor Immunology at SGPGIMS Lucknow for manuscript review and suggestions. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

## REFERENCES

1. No author listed. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. From the Commission on classification and terminology of the International League Against epilepsy. *Epilepsia* 1981;22:489-501.
2. No author listed. Proposal for revised classification of epilepsies and epileptic syndromes. Commission on Classification and Terminology of the International League Against Epilepsy. *Epilepsia* 1989;30:389-99.
3. Engel J Jr. International League Against Epilepsy (ILAE) A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: Report of the ILAE task force on classification and terminology. *Epilepsia* 2001;42:796-803.
4. Krishnamoorthy ES, Satishchandra P, Sander JW. Research in Epilepsy: Development Priorities for Developing Nations. *Epilepsia* 2003;44:5-8.
5. Gourie-Devi M, Gururaj G, Satishchandra P, Subbakrishna DK. Prevalence of neurological disorders in Bangalore, India: a community-based study with a comparison between urban and rural areas. *Neuroepidemiology* 2004;23:261-8.

6. Sridharan R, Murthy BN. Prevalance and pattern of epilepsy in India. *Epilepsia* 1999;40:631-6.
7. Manford M, Hart YM, Sander JW, Shorvon SD. The National General Practice Study of Epilepsy. The syndromic classification of the International League Against Epilepsy applied to epilepsy in a general population. *Arch Neurol* 1992;49:801-8.
8. Everitt AD, Sander JW. Classification of the epilepsies: time for a change? A critical review of the International Classification of the Epilepsies and Epileptic Syndromes (ICEES) and its usefulness in clinical practice and epidemiological studies of epilepsy. *Eur Neurol* 1999;42: 1-10.
9. Sawhney IM, Lekhra OP, Shashi JS, Prabhakar S, Chopra JS. Evaluation of epilepsy management in a developing country: a prospective study of 407 patients. *Acta Neurol Scand* 1996;94:19-23.
10. Jha S, Mathur VN, Mishra VN. Pitfalls in diagnosis of epilepsy of Janz and its implications. *Neurol India* 2002;50:467-9.
11. Mehndiratta MM, Aggarwal P. Clinical expression and EEG features of patients with juvenile myoclonic epilepsy (JME) from North India. *Seizure* 2002;11:431-6.
12. Benbadis SR, Tatum WO 4th, Gieron M. Idiopathic generalized epilepsy and choice of antiepileptic drugs. *Neurology* 2003;61:1793-5.
13. Vijai J, Cherian PJ, Stlaja PN, Anand A, Radhakrishnan K. Clinical characteristics of a South Indian cohort of juvenile myoclonic epilepsy probands. *Seizure* 2003;12:490-6.
14. No author listed. Guidelines for epidemiologic studies on epilepsy. Commission on Epidemiology and Prognosis, International League Against Epilepsy. *Epilepsia* 1993;34: 592-6.
15. Thomas SV, Kutty R 5th, Alexander A. Management and referral patterns of epilepsy in India. *Seizure* 1996;5:303-6.
16. Redhead K, Tasker P, Mumtaz A, Copsy G, Roberts P, Daws J, et al. Audit of the care of patients with epilepsy in general practice. *Br J Gen Pract* 1996;46:731-34.
17. Minshall, Smith D. The development of a city-wide epilepsy register. *Seizure* 2006;15:93-7.
18. Brodie MJ, Dichter MA. Antiepileptic Drugs. *N Eng J Med* 1996;334:168-75.
19. Joshi V, Katiyar BC, Mohan PK, Misra S, Shukla GD. Profile of epilepsy in a developing country: a study of 1,000 patients based on the international classification. *Epilepsia* 1997;18:549-54.
20. Sureka RK. Clinical profile and spectrum of epilepsy in rural Rajasthan. *J Assoc Physicians India* 1999;47:608-10.
21. Pillai J, Sperrling MR. Interictal EEG and the diagnosis of epilepsy. *Epilepsia* 2006;47 suppl 1:14-22.
22. No author listed. Randomised study of antiepileptic drug withdrawal in patients in remission. Medical Research Council Antiepileptic Drug Withdrawal Study Group. *Lancet* 1991;337:1175-80.



## Announcement

64<sup>th</sup> Annual Conference of Association of Physicians of India will be held from 29<sup>th</sup> January to 1<sup>st</sup> February, 2009, at India Expo Centre, Greater Noida, National Capital Region (NCR), it will be Hosted by API Ghaziabad Branch.

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