Clinico-Etiological Classification of Epilepsy in Children Presenting To Specialty Epilepsy Clinic at Tertiary Medical Centre

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Abstract
Objectives: To identify the clinical & etiological profile of children and the characteristics of seizures in them along with therapeutic responses.

Methods: All patients who attended the Epilepsy Clinic & fulfilled the selection criteria were enrolled in study. This is a descriptive study of 12 months & involved analysis of records of the patients who came to specialty OPD. Three groups were formed accordingly - focal, generalized & unknown onset with further etiological sub-divisions - Genetic, Structural/Metabolic, Immune, Infectious & Unknown.

Results: In all, 417 patients were studied. The distribution as per clinical presentation was- group I (generalized) 215 (58.5%), group II (focal) 154 (36.9%), group III (unknown) 48 (4.6%). The main etiologies were perinatal asphyxia (28.3%), NHBI (11.4%) in (structural-metabolic) sub group. In Genetic & Infectious, Channelopathies (10.3%) & Post Meningitis Sequelae (4.7%). 56.3% of the patient in group II were on more than 3 AEDs. 14.3% in group I were weaned of AEDs. 61.4% patients in group II were having neuro-developmental sequelae. EEG revealed abnormal activity in 30(6.2%) in group I & 31(19.3%) in group II. Maximum patient with refractory epilepsy were seen in group III.

Conclusion: To have a good management of epilepsy we need to have multi-dimensional classification of epilepsy based on both clinical & etiological spectrum. Perinatal Asphyxia & NHBI are one of the most common yet avertible etiologies.

Introduction
Epilepsy is one of the most urgent problems in pediatric neurology. Asserting the causes and types of seizure is important for diagnostic purposes and for evaluating therapy. In 2010 the ILAE defined focal as “originating within networks limited to one hemisphere. They may be discretely localized or more widely distributed. Focal seizures may originate in subcortical structures.” Generalized from onset seizures were defined as “originating at some point within, and rapidly engaging, bilaterally distributed networks.” Classifying a seizure as generalized does not rule out a focal onset obscured by limitations of our current clinical methods, but this is more an issue of correct diagnosis than of classification. A working distinction between focal and generalized onset is a practical one, and may change with advances in ability to characterize the onset of seizures. Clinicians have long been aware that so-called generalized seizures, for example, generalized absence with EEG generalized spike-waves, do not manifest equally in all parts of the brain. The ILAE emphasized the concept of bilateral, rather than generalized involvement of some seizures, since seizures can be bilateral without involving every brain network. The term “focal to bilateral tonic-clonic” was substituted for “secondarily generalized.” The term “generalized” was maintained for seizures generalized from onset. Clinicians commonly hear about tonic-clonic seizures for which the onset was unobserved. Perhaps, the patient was asleep, alone or observers were too distracted by the manifestations of the seizure to notice presence of focal features. There should be an opportunity to provisionally classify this seizure even in the absence of knowledge about its origin. The ILAE therefore allowed classification of any seizure type with the modifier “unknown onset.” It may be impossible to classify a seizure at all, either because of incomplete information or because of the unusual nature of the seizure [1-7].

Methods & Materials
Study type: Descriptive Analysis
Methodology: All patients who attended the Epilepsy Clinic & fulfilled the selection criteria were enrolled in study. This is a descriptive study of 12 months & involved analysis of records of the patients who came to specialty OPD. Three groups were formed accordingly - focal, generalized & unknown onset with further etiological sub-divisions - Genetic, Structural/Metabolic, Immune, Infectious & Unknown.

Enrollment Criterion
• Age less than 14 years at time of presentation to OPD.
• All patients who had seizures in last 1 year time period. 
• All patients who are on verge of developing epilepsy. 
• All patients presented to our epilepsy clinic based on clinical data combined with EEG and Neuroimaging and other auxiliary diagnosed as symptomatic Epilepsy. 
• Febrile seizures were not included

Strength of Study
258(62%) were male and 159(38%) were female subjects in our study.

We had further grouped our subjects into age groups in four age groups.
• 0 -12 months
• 1 year - 5 years
• 5 years -10 years
• >10 years

Only in last age group there was female pre-dominance.

Results & Discussion
In sub group Genetic, Channelopathies (10.5%) and in sub group Infectious, Neuro-cysticercosis and Post Meningitis Sequelae (4.7%) were significant etiologies. In structural and metabolic subgroups perinatal asphyxia (hypoxic ischemic encephalopathy) and Neonatal hypoglycemia brain injury (NHBI) were the major etiologies. In Immune sub-group, few cases of auto-immune encephalitis were also there. MTLS was major etiology in unknown/syndromic constellations. MTLS (Mesial Temporal Lobe Sclerosis) was most common in unknown origin group. Neurological examination is usually normal with the exception of memory deficits. Inter-ictal electroencephalogram (EEG) findings in patients with MTLE typically include unilateral or bilaterally-independent mesial tem-poral spikes, best seen with basal (sphenoidal, inferior tem-poral) derivations. Ictal EEG recordings usually reveal ictal onset consisting of rhythmic 5 to 7 Hz activity in one mid-inferomesial temporal region, but there may be variations in this pattern. High-resolution MRI often demonstrates unilateral or bilateral hippocampal atrophy associated with hyper-intense T2 signal in one or both hippocampi sometimes extending to amygdala or other medial temporal structures. These findings are highly specific for MTS. Post Tuberculous mening-encephalitis, development of Epilepsy was also present in our study with 4.7% (21) patients having sequelae in form of seizure disorder.

Refractory Epilepsy
Our study included failure to achieve seizure control with two or more AEDs with adequate dosage and posology. In group I (Generalised), cases of refractory epilepsy were least comparing to other two groups. Sodium Valproate and Carbamazepine being the 1st line therapy, Phenytoin as 2nd line and Leviteracetam/Topiramate/Zonisamide being 3rd line in our facility. In Group I, most of the patients were managed on only Valproate.

Eeg Analysis
Abnormal epileptiform activity was evident maximum in group 3 (unknown onset). 74% of the children in group 3 had abnormal EEG. These patients were also having refractory epilepsy more in common. However, in numerical assessment maximum patients having abnormal EEG were from group 2 (focal) in our facility. 32% of children had some form of abnormal activity. Inspite of the fact that maximum patients formed the group 1, eeg analysis was normal mostly in this group with fair prognosis.

Neurodevelopment Sequelae
Neurodevelopment is a term referring to the brain’s development of neurological pathways that influence performance or functioning (e.g., intellectual functioning, reading ability, social skills, memory, attention or focus skills). Neuro-development sequelae assessment included gross motor development, behavioral difficulties, speech and personal social domain of development. In Group 3, there was maximum percentage of subjects with such sequelae. In Etiological Sub-group, Metabolic sub group had maximum subjects with such sequelae resulting from perinatal insult mostly.

Response to Therapy
Patients were weaned off AEDs earlier and successfully in Group 1 (Generalised) in our facility. For Therapeutic response in this, compliance was main key. Most of the patients were in either Valproate alone or Valproate with Leviteracetam along with Clobazam. In group 2, patients were mostly on carbamazepine and valproate combination therapy. There was very little response to the treatment in group 3 (unknown).

Trends of Aeds
Sodium Valproate is most commonly used AED along with Carbamazepine. Addition of Leviteracetam as 2nd line AED had resulted in better control of seizures in our facility.

Discussion on major etiologies
Neonatal Hypoglycemic Brain Injury
Neonatal hypoglycemia (<46 mg/dL) occurs in 5% to 15% of Normal term neonates and can cause visual impairment, epilepsy, and cognitive deficits. Numerous animal and human studies have suggested that neonatal hypoglycemia in the context of HIE may be more detrimental than either condition alone. Neuroimaging studies in neonatal hypoglycemia have shown a correlation between hypoglycemia, parieto-occipital injury, and involvement of the underlying white matter tracts, corpus callosum, and thalamus.
Encephalopathy was one of the major causes of epilepsy in our study. Early neonatal period can alleviate NHBI. Hypoxic Ischemic Encephalopathy is a condition that occurs in newborns soon after delivery and monitoring of vitals in early neonatal period can alleviate NHBI. Hypoxic Ischemic Encephalopathy indeed, seizure is a feature of moderate to severe HIE.

Seizures occur in many infants who have sustained a significant hypoxic-ischemic insult indeed, seizure is a feature of moderate and severe HIE. In general, the more severe or prolonged the hypoxia-ischemia, the more seizure activity the infant will have. There has been considerable debate as to whether seizure activity after a hypoxic-ischemic event confers an additional risk factor on the infant in terms of adverse neurodevelopmental outcome.

The prognosis for children with HIE depends on the severity and duration of the neurologic abnormality. Major Neuro development problems occur only after moderate and severe HIE, and death is a significant risk in severe HIE. Emerging data strongly support the observations that a significant number of children with perinatal hypoxic-ischemic insult previously considered to be without major problems do have significant perceptual-motor difficulties or a reduction in cognitive abilities [8-15].

Cerebral palsy and epilepsy were seen in 47% and 65% of babies with hie grade 2 and 3 injury.

**Conclusion**

To have a good management of epilepsy we need to have multidimensional classification of epilepsy based on both clinical & etiological spectrum. Perinatal Asphyxia & NHBI both were one of the most common yet avertible etiologies. Early Breastfeeding of newborn soon after delivery and monitoring of vitals in early neonatal period can alleviate NHBI. Hypoxic Ischemic Encephalopathy was one of the major causes of epilepsy in our facility. Prognosis depends on multiple factors including early intervention with physiotherapy.

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**References**


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