CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS WITH EPILEPTIC ENCEPHALOPATHY : A HOSPITAL BASED STUDY

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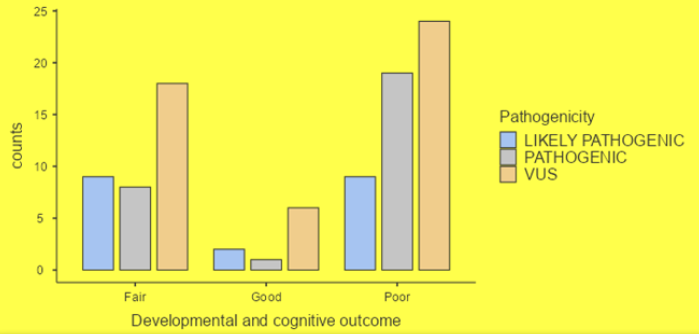
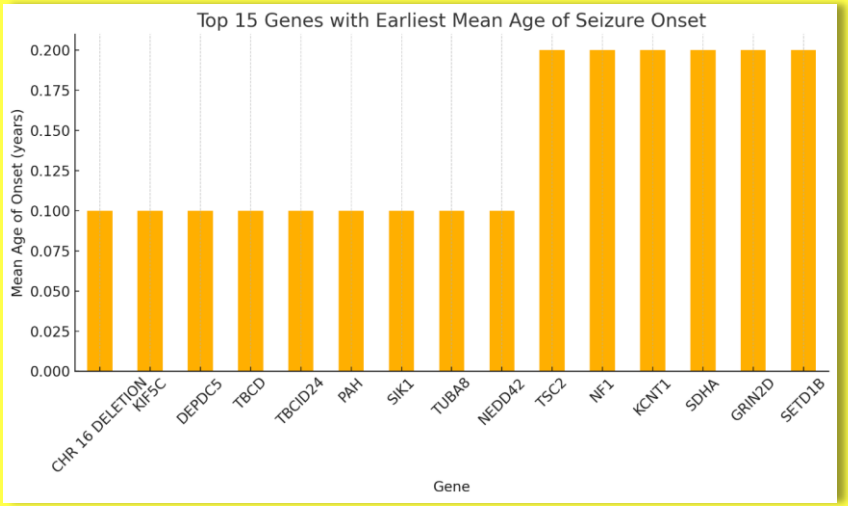
- **Aim**: To evaluate the clinical spectrum and etiological profile of patients with epileptic encephalopathy, with a specific focus on genetic findings, in a hospital-based cohort of 200 patients.
- **Materials** : Retrospective hospital-based study at Department of Neurology at NIMHANS .
- **Methods**: Retrospective, hospital-based study at NIMHANS (Jan 2015–Feb 2025) including 200 epileptic encephalopathy patients; ethics approved with informed consent.

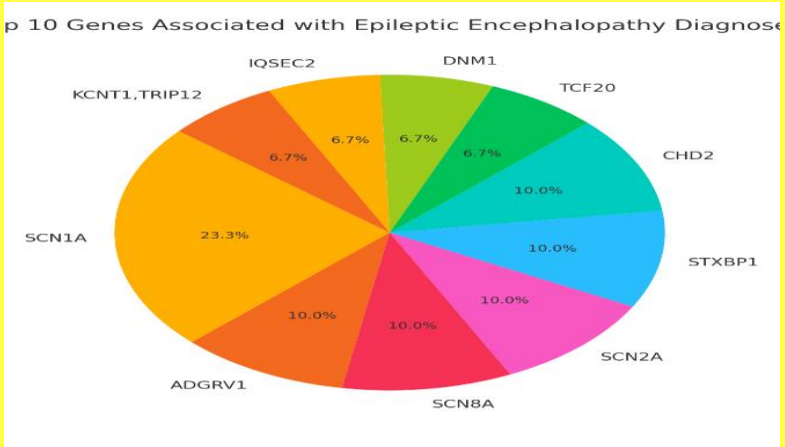
  Data came from registries/EMU/video-EEG and a structured proforma capturing onset, semiology, ILAE-read EEG, MRI categories, treatments, and outcomes was done .Genomics (n=96): tiered NGS—pre-2022 targeted 180-gene panel; from 2022 trio-WES; Illumina 2×150 bp; GRCh38/BWA-MEM/GATK pipeline. Analysis in SPSS/R using appropriate parametric/non-parametric tests, χ^2/Fisher for categorical data, and logistic regression for predictors of seizure freedom/developmental outcome.

- **Results**

- Among 200 epileptic encephalopathy (EE) patients, genetic reports were available for 96, spanning 74 genes. The cohort was young (mean age 3.85 years; median 2.5) with very early seizure onset (mean 1.16 years; median 0.60); distributions were non-normal. The earliest mean onsets (~0.1 year) occurred with chr16 deletion, KIF5C, DEPDC5, TBCD, and TBC1D24; intermediate/later onsets were seen with DROSHA (3 y), STAG1 (4 y), CUX1 (7 y) and EEF1A2 (12 y). SCN1A was most frequent (Dravet n=4 plus EIEE/LGS/unspecified), with recurrent associations for STXBP1→DEE, SCN8A→DEE/LKS, SCN2A→DEE/LGS/West, and CHD2→LGS/West. Variant classes were: pathogenic 29.2%, likely pathogenic 20.8%, and VUS 50.0%; VUS presented at older ages and with later onset. Syndromic diagnoses were dominated by DEE (36.5%); LGS (14.6%) and unclassified EE (20.8%) were also common. Inheritance was chiefly autosomal dominant (78.1%), then autosomal recessive (18.8%). EEG showed predominantly slow backgrounds and multifocal discharges; sleep architecture was abnormal/absent in most. MRI abnormality rates did not differ by pathogenicity; atrophy was the commonest lesion. Steroid response varied by pathogenicity (p=0.041) and strongly tracked seizure control (p<0.001), whereas AED count/response and seizure frequency showed no intergroup differences. On multivariable analysis, poor developmental/cognitive outcomes were independently associated with slow VEEG background (p=0.021) and absent sleep structures (p=0.011). Among the 104 patients without available genetic reports, the **mean age at seizure onset was 1.4 years (IQR 0.6–2.5)**. The most common seizure type was **generalized tonic–clonic seizures (42%)**, followed by **epileptic spasms (28%)**, focal seizures with impaired awareness (20%), and myoclonic seizures (10%). On video-EEG, the predominant abnormalities were **slow background activity (82%)** and **multifocal epileptiform discharges (65%)**, with hypsarrhythmia in 18% reflecting West syndrome. Treatment responses showed that **steroids produced >50% seizure reduction in 38%**, while anti-seizure medications alone achieved sustained seizure control in only 15%. Developmentally, **severe delay was present in 72%**, moderate delay in 18%, and only 10% retained near-normal milestones. Seizure outcome was poor, with **>70% continuing to have daily seizures** despite polytherapy, underscoring the refractory nature of EE in this subgroup.







- **Conclusion:**

- This decade-long hospital-based study highlights the heterogeneous clinical and etiological spectrum of epileptic encephalopathies. Genetic testing identified pathogenic or likely pathogenic variants in nearly half of tested patients, with *SCN1A*, *STXBP1*, *SCN2A* and *SCN8A* being the most frequently implicated genes. Patients without genetic data demonstrated similar early onset, refractory seizures, and profound developmental impairment, emphasizing the overall severity of EE regardless of etiology. Steroid responsiveness was a significant predictor of seizure control, while slow background and absent sleep structures on VEEG independently predicted poor developmental outcomes. These findings underscore the importance of integrating genomic diagnostics with detailed electroclinical phenotyping to guide prognosis, optimize management, and expand access to genetic testing in resource-limited settings.

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