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Etiopathogenesis of Drug-Refractory Epilepsy in Children (2 Months To 18 Years): A Tertiary Care Study

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Abstract: ***Background: Drug-refractory epilepsy (DRE) affects nearly 30% of pediatric epilepsy cases, leading to significant morbidity. Aim: To evaluate etiopathogenesis, clinical risk factors, and treatment response in children with DRE aged 2 months to 18 years. Methods: Cross-sectional observational study conducted over 6 months at a tertiary care hospital. Fifty patients meeting ILAE criteria for DRE were analyzed. Data included demographic profile, seizure onset, risk factors, imaging, EEG, and comorbidities. Results: Mean age was 9.8 years; 68% were male. Structural etiologies (60%) predominated, followed by genetic (18%), infectious (6%), metabolic (4%), immune-mediated (2%), and unknown (10%). Birth asphyxia (50%) was the leading perinatal risk factor. 80% had NICU stay history. Major comorbidities were global developmental delay/intellectual disability (56%) and cerebral palsy (23%). Conclusion: Preventable perinatal insults (asphyxia, prematurity, NICU complications) remain the strongest predictors of pediatric DRE in India. Early neuroimaging, genetic counseling, and tailored polytherapy are essential.***

Keywords: pediatric epilepsy, drug-refractory epilepsy, perinatal risk factors, structural etiology, developmental delay

1. Introduction

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures resulting from abnormal electrical activity in the brain. It is one of the most common neurological conditions globally, affecting individuals of all ages. According to the World Health Organization (WHO), approximately 50 million people worldwide are living with epilepsy, with nearly 80% of them residing in low- and middle-income countries (LMICs), where access to diagnosis and treatment remains suboptimal.

A subset of individuals with epilepsy do not respond adequately to standard anti-seizure medications (ASMs). This condition is termed drug- resistant epilepsy (DRE), defined by the International League Against Epilepsy (ILAE) as failure of adequate trials of two appropriately chosen and tolerated ASMs (whether as monotherapy or in combination) to achieve sustained seizure freedom. DRE affects approximately 20–30% of children with epilepsy and is associated with increased risk of cognitive impairment, psychiatric comorbidities, injury, and reduced quality of life.

In India, the burden of pediatric DRE is particularly challenging due to late presentation, high rates of symptomatic etiologies (e.g., perinatal insults, CNS infections), and limited access to specialized epilepsy care and surgical interventions. Addressing this burden requires comprehensive epidemiological insights and targeted health system strategies.

Aims and Objectives

1) To determine the clinical and treatment profile of children with drug-resistant epilepsy.
2) To identify risk factors associated with refractory epilepsy.
3) To evaluate the pattern of AED usage and treatment failure.
4) To assess predictors such as age of onset, developmental delay, family history, and imaging findings.

2. Methodology

Design: Cross-sectional observational study.

Duration: 6 months.

Setting: Tertiary care teaching hospital, Gujarat.

Population: 50 children (2 months–18 years) fulfilling ILAE 2010 definition of DRE.

Inclusion Criteria: ≥2 failed AED trials with good compliance.

Exclusion: Acute symptomatic seizures, incomplete records.

Tools: Pre-validated forms documenting demographics, seizure type, EEG, MRI, AED response, comorbidities. Genetic testing was advised selectively.

Statistical Methods: Descriptive statistics; Chi-square for categorical associations; logistic regression for predictors of DRE.

3. Results

Table 1

Risk Factor	Frequency (%)
Birth Asphyxia	25 (50%)
Neonatal Jaundice	3 (6%)
Hypoglycemia	5 (10%)
CNS Infections	3 (6%)
Fever-related Seizures	8 (16%)
Others	7 (14%)

Table 2

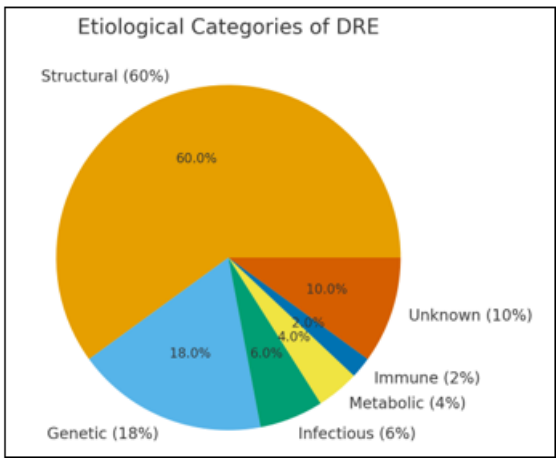
NICU Stay	Number (%)
Present	40 (80%)
Absent	10 (20%)

Table 3

Etiology	Cases (n=50)	Percentage (%)
Structural	30	60%
Genetic	9	18%
Infectious	3	6%
Metabolic	2	4%
Immune-mediated	1	2%
Unknown	5	10%

Table 4

Comorbidity	Cases (n=39)	Percentage (%)
Global Developmental Delay/ID	22	56%
Cerebral Palsy	9	23%
Behavioural Issues/ASD	4	10%
Hemiparesis/Ataxia	3	8%
Encephalopathy	1	3%



4. Discussion

Structural etiologies (notably perinatal asphyxia and cortical malformations) accounted for the majority, consistent with global and Indian studies. Preventable perinatal events remain a dominant cause, highlighting the importance of strengthening obstetric and neonatal care. Genetic contributions (18%) echo advances in precision neurology but remain under-diagnosed due to financial barriers. High comorbidity rates (GDD, CP) emphasize the neurodevelopmental burden of DRE. Early NICU insults strongly predicted poor outcomes, aligning with ILAE predictors.

5. Conclusion

Pediatric drug-refractory epilepsy in India is driven primarily by structural and perinatal causes. Policy interventions should prioritize:

1) Improved perinatal care to prevent hypoxic-ischemic insults.
2) Early imaging and genetic evaluation for precise etiological diagnosis.
3) Rational polytherapy with newer AEDs (clobazam, lamotrigine) tailored to etiology.
4) Multidisciplinary management addressing comorbidities.

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