Original Article

Clinical and Electroencephalogram Patterns of Refractory Epilepsy in Children

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ABSTRACT

Introduction: *Refractory epilepsy, impacting 10–20% of children with epilepsy, significantly affects the child's education, social interactions, cognitive function, and recreational activities. A thorough clinical assessment can unveil precise syndromic and etiological diagnoses. Recent strides in neuroimaging and electrophysiology have transformed the management, complementing clinical evaluation.* ***Aim of the study:*** *This study aimed to assess the clinical and electroencephalogram patterns of refractory epilepsy in children.* ***Methods & materials:*** *This prospective observational study was conducted at the Department of Pediatric Neurology, Combined Military Hospital, Dhaka, Bangladesh from July 2022 to June 2023. A total of 42 diagnosed cases of refractory epilepsy were selected as study subjects using a purposive sampling technique. Data collection was conducted using MS Office tools.* ***Results:*** *This study found that 50% of cases had syndromic epilepsy, 33% had symptomatic epilepsy, and 74% had onset within the first year. Episodes lasted minutes and occurred over 5 times annually. Regarding EEG findings, consistent with generalized epileptogenic activity was observed in the highest number of cases (28.58%). 14.29% of cases showed generalized tonic-clonic seizure. In the*

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current study, diagnostic findings revealed that the highest number of cases (33.33%) had infantile spasms. Additionally, 16.67% and 9.52% of cases were identified with seizure disorder and refractory epilepsy with tuberous sclerosis, respectively. ***Conclusion:*** *Among children with refractory epilepsy, syndromic epilepsy is most prevalent. To pinpoint distinctive features such as generalized tonic-clonic seizures, epileptogenic activity, infantile spasms, and epileptic encephalopathy, the electroencephalogram (EEG) emerges as a highly effective diagnostic tool.*

Keywords: *Clinical pattern, Electroencephalogram, Refractory epilepsy, Children, Seizure, Infantile spasm*

INTRODUCTION

Epilepsy, a chronic neurological disorder affecting approximately 50 million individuals globally, stands as a significant public health concern according to the World Health Organization (WHO) [1]. Despite its historical recognition, the condition is often accompanied by widespread misinterpretation, discrimination, and social stigma [2]. These societal challenges compound the difficulties faced by those with epilepsy, contributing to a cycle of misconceptions and difficulties in social integration. Moreover, epilepsy not only inflicts the burden of a chronic medical condition but also predisposes individuals to potential injuries and premature mortality, amplifying its impact. The repercussions extend beyond the affected individuals to encompass their families and the broader society. The consequences include a diminished quality of life and financial hardship, creating a ripple effect that permeates various aspects of life. In terms of global health, epilepsy constitutes 0.5% of the overall burden of disease [3]. Strikingly, this condition is not evenly distributed, with a significant majority of those affected—80%—residing in developing countries. This highlights the existence of disparities in access to healthcare resources, education, and awareness, further exacerbating the challenges faced by individuals living with epilepsy in these regions. A substantial portion of epilepsy cases, at least 50%, manifests during childhood or adolescence, underscoring the significant impact on the developmental years of individuals [4]. Although epilepsy can arise at any age, its prevalence is notably pronounced in younger populations, emphasizing the importance of addressing the condition in the context of childhood and adolescence. A recent comprehensive review encompassing 23 Asian countries, including Bangladesh, shed light on the epidemiological landscape of epilepsy. The findings revealed a wide-ranging lifetime prevalence of epilepsy, varying from 1.5 to 14.0 per 1000 population [5]. This diversity underscores the need for targeted interventions that consider regional disparities in healthcare accessibility, awareness, and resources. Notably, individuals with epilepsy in developing countries, such like Bangladesh, often encounter significant challenges in accessing effective treatment [6]. The chronic nature of the condition compounds this issue, as many patients either discontinue treatment or face barriers such as the unaffordability of medication. Consequently, a considerable proportion of epilepsy cases persist

without proper management, contributing to what is known as the epilepsy treatment gap. This treatment gap is a global phenomenon, transcending economic boundaries. Even in high-income countries, it hovers around 10%, while in low-income countries, such as those in the developing world, it can soar up to 75% [7]. These figures underscore the urgent need for concerted efforts on a global scale to bridge this gap, ensuring that individuals with epilepsy receive the necessary care regardless of their economic status. Research on epilepsy in Bangladesh has primarily focused on small communities [8,9] or hospitals [10,11]. However, as of now, there is a lack of a nationally representative study on epilepsy in Bangladesh, which is crucial for informing comprehensive programs and policies related to the condition.

METHODS & MATERIALS

This was a prospective observational study that was conducted at the Department of Pediatric Neurology, Combined Military Hospital, Dhaka, Bangladesh from July 2022 to June 2023. The study included 42 cases diagnosed as refractory epilepsy patients, selected through purposive sampling. Trained physicians with a background in neurology confirmed the diagnosis of suspected epilepsy cases identified through interviewer-administered questionnaires. EEG (Electroencephalogram) was performed for all of the participants. Ethical approval for the study was obtained from the hospital's ethical committee, and written consent was obtained from all participants before data collection. Demographic and clinical information of the participants was recorded, and data were processed, analyzed, and disseminated using MS Office tools.

RESULT

In this study, 62% of cases were female, 38% male, with 49% from the >3 years age group. Delivery methods included 62% Lower Uterine Segment Caesarean Section (LUCS) and 38% Normal Vaginal Delivery (NVD). The majority (83%) delivered at home at term. Perinatal asphyxia indicated 29% with neonatal seizures and 7% with neonatal sepsis. Family history showed 90% had consanguinity, while febrile seizure and epilepsy were found in 10% and 7%, respectively. Developmental history indicated 5% each for delayed speech, delayed vision, and delayed hearing. Regarding epilepsy type, 50% had syndromic epilepsy, and 33% had symptomatic epilepsy **[Table-I]**.

Table I: Etiological factors of patients (N=42)

Characteristics	n	%
Gender		
Female	26	62%
Male	16	38%
Age (years)		
<1	**11**	26%
1-3	14	33%
>3	17	49%
Delivery mode		
NVD	16	38%
LUCS	26	62%
Place of deliver		
Home	7	17%
Hospital	35	83%
Time of delivery		
Term	34	81%
Preterm	8	19%

Complication at delivery		
Perinatal asphyxia	33	74%
Neonatal sepsis	3	7%
Neonatal seizure	12	29%
Family history		
Consanguinity	38	90%
F/H of epilepsy	3	7%
Febrile seizure	4	10%
Developmental history		
Delayed speech	2	5%
Delayed vision	2	5%
Delayed hearing	2	5%
Type of epilepsy		
Syndromic	21	50%
Genetic	5	12%
Symptomatic	14	33%
NMD	3	7%
Idiopathic	5	12%

NVD: Normal Vaginal Delivery, LUCS: Lower Uterine Segment Caesarean Section

Analyzing the clinical pattern of seizures, it was observed that nearly three-fourths of the cases (74%) had an onset time of less than 1 year. Additionally, 17% and 10% of cases were found with onset times of 1-3 years and > 3 years, respectively. The majority of seizures were of the generalized type (83%), followed by focal (14%) and both types (2%). In terms of nature, tonic seizures were predominant (64%), with myoclonic and clonic seizures observed in 43% and 31% of cases, respectively. Most cases reported that epilepsy episodes lasted for minutes and occurred more than 5 times in a year **[Table-II]**.

Table II: Clinical pattern regarding seizure

Categories	**n**	**%**
Time of 1st onset		
Less than 1 year	31	74%
1-3 years	7	17%
> 3 years	4	10%
Type of seizure		
Generalized	35	83%
Focal	6	14%
Both	1	2%
Nature (18 cases had multiple nature)		
Myoclonic	18	43%
Tonic	27	64%
Clonic	13	31%
Duration		
Seconds	8	19%
Minutes	40	95%
Frequency		
≤ 5 times	20	48%
> 5 times	22	52%

Meditation (TM) identified GLUT1 deficiency syndrome in 5%, nicotinamide adenine dinucleotide deficiency in 2%, and 10% were not done. In more than 5% of cases, unremarkable MRI, bilateral cerebral atrophy with gliosis, and periventricular leukomalacia with moderate atrophy were observed **[Table-III]**.

The CT scan revealed unremarkable findings in 5% of cases. Benign enlargement of the subarachnoid space in infancy in 7%. Additionally, old infarct in the left cerebral hemisphere, mild cerebral atrophy, and soft calcifications in the para ventricular region in both cerebral hemispheres were found in 2% each. Whole-exome sequencing (WES)/Transcendental

Table III: Clinical investigation of CT scan, MRI, and WES/TMS

Variables	%
CT scan	
Benign enlargement of the subarachnoid space in infancy	7
Old infarct in the left cerebral hemisphere, mild cerebral atrophy	2
Soft calcifications in the para-ventricular region in both cerebral hemispheres	2
Unremarkable findings	5
Whole-exome sequencing (WES) / Transcendental meditation (TM)	
GLUT 1 deficiency syndrome	5
Nicotinamide adenine dinucleotide deficiency	2
Not done	10
MRI of Brain	
Tuberous sclerosis	2
Cerebral atrophy	10
Bilateral cerebral atrophy with gliosis	7
Chronic hematoma in RT thalamus and occipital horns	5
Agenesis of corpus callosum	2
Hypoxic ischemic encephalopathy	5
Periventricular leukomalacia with moderate atrophy	7
Obstructive hydrocephalus	2
Medial and temporal obstructive hydrocephalus (Right)	2
Poly-microgyria (Bilateral)	2
Relative hypo-perfusion in both temporal lobes	2
Unremarkable MRI	7

Regarding EEG findings, consistent with generalized epileptogenic activity was observed in the highest number of cases (28.58%). 14.29% of cases showed generalized tonic-clonic seizure **[Table-IV]**.

Table IV: EEG (Electroencephalogram) pattern description for refractory epilepsy

EEG Findings	n	%
Generalized tonic–clonic seizure	6	14.29%
Consistent with epileptogenic activity	5	11.90%
Consistent with epileptic spasm	4	9.52%
Consistent with generalized epileptogenic activity	12	28.58%

Consistent with infantile spasm	4	9.52%
Consistent with epileptic encephalopathy	4	9.52%
Focal epileptogenic activity	2	4.76%
Multifocal epilepsy	3	7.14%
Sporadic epileptiform discharge	1	2.38%
Normal	1	2.38%

In the current study, diagnostic findings revealed that the highest number of cases (33.33%) had infantile spasms. Additionally, 16.67% and 9.52% of cases were identified with seizure disorder and refractory epilepsy with tuberous sclerosis, respectively **[Table-V]**.

Table V: Diagnostic findings among the participants

Diagnosis	n	%
Infantile spasm	14	33.33
Ohtahara syndrome	2	4.76
Seizure disorder with developmental delay, microcephaly, and moderate ASD	3	7.14
Seizure disorder	7	16.67
Refractory epilepsy with tuberous sclerosis	4	9.52
Refractory epilepsy with Rasmussen encephalitis	2	4.76
West syndrome with GDD	3	7.14
Refractory epilepsy with spastic quadriplegia	2	4.76
Refractory epilepsy with focal status epilepticus, ADHD, and chronic hematoma thalamus	3	7.14
Refractory epilepsy due to corpus callosal agenesis	2	4.76
Total	42	100

DISCUSSION

In this study, 62% of cases were female, and 38% were male, with 49% in the >3 years age group. Another study indicated a prevalence in children aged <18 years [12]. Delivery methods included 62% LUCS and 38% NVD, with 83% of cases delivering at home at term. Phrenic nerve activity showed that 29% had neonatal seizures, and 7% had neonatal sepsis. Regarding family history, 90% had consanguinity, while febrile seizure and epilepsy were found in 10% and 7% of cases [12]. Regarding developmental history, 5% of cases each had delayed speech, delayed vision, and delayed hearing. In terms of epilepsy type, 50% had syndromic epilepsy, and 33% had symptomatic epilepsy. Another study found a similar gender distribution, with 62% female and 38% male participants [13]. Adverse perinatal events (48%) and CNS infection sequelae (24%) were identified as major causes of refractory epilepsy in a study by Chawla et al. [14]. Analyzing seizure patterns, 74% had onset within the first year, while 17% and 10% had onset at 1-3 years and >3 years, respectively. Types of seizures included generalized (83%), focal (14%), and both (2%). In terms of nature, tonic seizures were prevalent in 64% of cases. Moreover, myoclonic and clonic seizures were present in 43% and 31% of cases, respectively. Epilepsy typically lasts for minutes and occurs more than 5 times a

year in most cases. Another study revealed that 61.12% of patients had unclassified seizures, followed by 29.5% with generalized seizures and 9% with partial seizures [15]. CT scan results showed unremarkable findings in 5% of cases, while old infarct in the left cerebral hemisphere, mild cerebral atrophy, and soft calcifications in the para ventricular region in both cerebral hemispheres were found in 2% each. In terms of whole-exome sequencing (WES)/Transcendental Meditation (TM), 5% had GLUT1 deficiency syndrome, 2% had nicotinamide adenine dinucleotide, 2% had benign enlargement of the subarachnoid space in infancy, and 10% were not done. More than 5% of cases showed unremarkable cerebral artery, bilateral cerebral atrophy with gliosis, and periventricular leukomalacia with moderate atrophy. In a previous study, MRI showed positive findings in all 28 patients with positive etiology (100%), while the CT scan was positive in 11 patients (39.2%) [13]. Regarding EEG findings, the highest number of cases were consistent with generalized epileptogenic activity (28.58%) and 14.29% exhibited generalized tonic-clonic seizures. Additionally, more than 10% of cases showed findings consistent with epileptogenic activity (11.90%). Similar findings were observed in another study [16]. In the current study, diagnostic findings revealed that the highest number of cases (33.33%) had infantile spasms. Furthermore, 16.67% and 9.52% of cases were identified with seizure disorder and refractory epilepsy with tuberous sclerosis, respectively. Another study reported that 69% of children developed spasms within 3 months to 1 year of age, with a mean age at the first and last examination being 10.9 months and 2.1 years, respectively [17].

LIMITATION OF THE STUDY

This study was conducted at a single center with a limited sample size. Moreover, there was limitation of genetic testing. Additionally, the study was carried out over a brief period, and therefore, the findings may not accurately represent the overall situation in the entire country.

CONCLUSION & RECOMMENDATION

Among children with refractory epilepsy, syndromic epilepsy is most prevalent. To identify specific features such as generalized tonic-clonic seizures, epileptogenic activity, infantile spasms, and epileptic encephalopathy, the electroencephalogram (EEG) serves as a highly effective diagnostic tool. This specialized approach enables a nuanced understanding of refractory epilepsy in children, assisting clinicians in customizing targeted interventions for improved management and outcomes.

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CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee

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