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Clinical, Neuroimaging and Electroencephalographic Characteristics of Pediatric Medically Intractable Epilepsy

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Abstract

Objectives: to investigate the clinical, neuroimaging, and electroencephalographic characteristics of pediatric medically intractable epilepsy in order to predict and overcome this intractability. **Methods:** We conducted a prospective case-control study with 50 participants, divided into a study group of 25 patients with refractory epilepsy and a control group of 25 epileptic children with good control of seizures. All participants underwent a comprehensive assessment, including medical history, physical examination, neuroimaging, neurophysiological evaluation, and metabolic workup. **Results:** The study revealed that total number of patients was 50 (25 case 12 male & 13 female and 25 control 11 male & 14 female). Children with refractory epilepsy had abnormal neuroimaging. Additionally, the interictal EEG monitoring showed more frequent epileptiform discharges in the refractory group. **Conclusions:** It is important to evaluate pediatric patients with medically intractable epilepsy. Abnormal development, neuroimaging and frequent epileptiform discharges on EEG may indicate a higher likelihood of refractory epilepsy for further research with large number.

Keywords: Clinical, Neuroimaging, Electroencephalographic, Epilepsy, Medically Intractable.

1. Introduction:

Epilepsy, one of the oldest known diseases, has been surrounded by fear, ignorance, prejudice, and social stigma throughout history. Sadly, in numerous countries, this stigma continues to persist, greatly impacting the well-being of individuals affected by the condition, especially children and their families. Epilepsy stands as one of the most challenging disorders in childhood. Thankfully, a significant portion of patients can be successfully treated and achieve positive outcomes. Nevertheless, approximately 10 to 30% of people with epilepsy experience resistance to treatment, a condition referred to as "intractable seizures." [1].

Intractable epilepsy is defined by seizures that persist despite maximally tolerated dosages of more than two anti-Intractable epilepsy is characterized by seizures that continue to occur despite the administration of the highest tolerated doses of two or more anti-epileptic medications. It is further defined by the occurrence of an average of at least one seizure per month over a period of 18 months, with no seizure-free interval lasting longer than three months within this 18-month timeframe [2].

Several prospective studies have been conducted to investigate risk factors associated with refractory epilepsy (RE). These studies varied in their sampling methods, including population-based and hospital-based approaches, and also differed in terms of including children, adults, or both in their samples. However, no single factor has been identified as essential for precise prediction. The presence of one or more of these symptoms can aid in identifying individuals who are unlikely to respond to medical treatment.

Intractable epilepsy poses a significant health burden in various regions across the globe. When epilepsy remains persistent and untreated, it can lead to severe medical consequences, such as an elevated risk of mental illnesses, physical harm, and premature mortality. Additionally, intractable seizures impose a substantial financial burden on society [3].

Emphasizing the importance of timely identification of refractoriness, it is crucial to prioritize the detection of this condition before considering alternative treatments like surgery. Early surgical intervention, when successful, has the potential to prevent or reverse the emotional and cognitive impacts of uncontrolled seizures, especially during critical developmental periods [4].

This study was planned to study the clinical profile, neuroimaging (CT & MRI) and electrophysiological characteristics of medically intractable seizures in children in order to predict and know how to overcome this intractability.

2. Methods

In this prospective case-control study, we recruited participants from the pediatric inpatient department and outpatient pediatric neurology clinic of Benha University Hospital. The study was conducted between May 2021 and May 2022.

The study was done after being approved by the institutional ethical committee, Faculty of Medicine, Benha University and informed consent was obtained from all the participants' parents.

The study included 50 participants divided into two groups: the study group and the control group. There were 25 individuals with refractory epilepsy in the study group. These patients were attending Benha University Hospital's paediatric department and outpatient pediatric neurology clinic.

The control group was comprised of 25 epileptic youngsters whose seizures had been well-controlled over the preceding 18 months.

To be included in the study, patients had to meet the following criteria: children from 1 to 18 years old of both sexes who were diagnosed with intractable epilepsy.

Children with poor compliance to anti-epileptic drugs and children whose parents were not willing to participate in the study were excluded from the study.

Statistical analysis

Statistical analysis was performed using SPSS version v26 (IBM Inc., Chicago, IL, USA). A comparison between the two groups was conducted using an unpaired Student's t-test, and the mean and standard deviation (SD) values were reported. For qualitative variables, frequency and percentage (percent) were presented, and the Chi-square or Fisher's exact test was employed for analysis when applicable. A two-tailed P value of 0.05 or less was considered statistically significant.

3. Results

Age and sex were insignificantly different between the refractory epilepsy and the control groups. The most common age of onset was 1 month- 2 years (40%), while the least common age of onset was 12 years – 18 years (8%) in the refractory epilepsy group. The most common age of onset was 2- 12 years (60%), while the least common age of onset was 1 month (4%) in the control group. Age of onset of seizures and type of seizures were insignificantly different between the studied groups. **Table 1**

Table (1) Socio-demographic data, Age of onset of and types of seizures of the refractory epilepsy and control groups

Variable		Cases of refractory epilepsy N=25		Controls N=25		Test of sig	P
Age (years)	**Mean ±SD**	7.34 ± 4.45		7.34 ± 4.02		Z_{MWU}= 1.09	0.9 (NS)
		No.	**%**	**No.**	**%**	X^2 test	
Sex	**Male**	12	48.0	11	44.0	3.6	0.7 (NS)
	Female	13	52.0	14	56.0		
Age of onset of seizures							
First month		5	18.0%	1		4.0%	0.09
1 month- 2 years		10	42.0%	7		28.0%	(NS)
2 years – 12 years		8	32.0%	15		60.0%	
12 years – 18 years		2	8.0%	2		8.0%	
Type of seizures							
Generalized		19	76	21		84.0	0.6
Focal		6	24	4		16.0	(NS)

Z_{MWU}= Z value of Mann Whitney U test

The neurological examination was abnormal in 52% of patients with hypertonia & hyper reflexia was the commonest (32%), and normal in 48% of patients in the refractory epilepsy group. **Figure 1** reveals that statistically non-significant difference in study group regarding Neurological examination. **Figure 1**

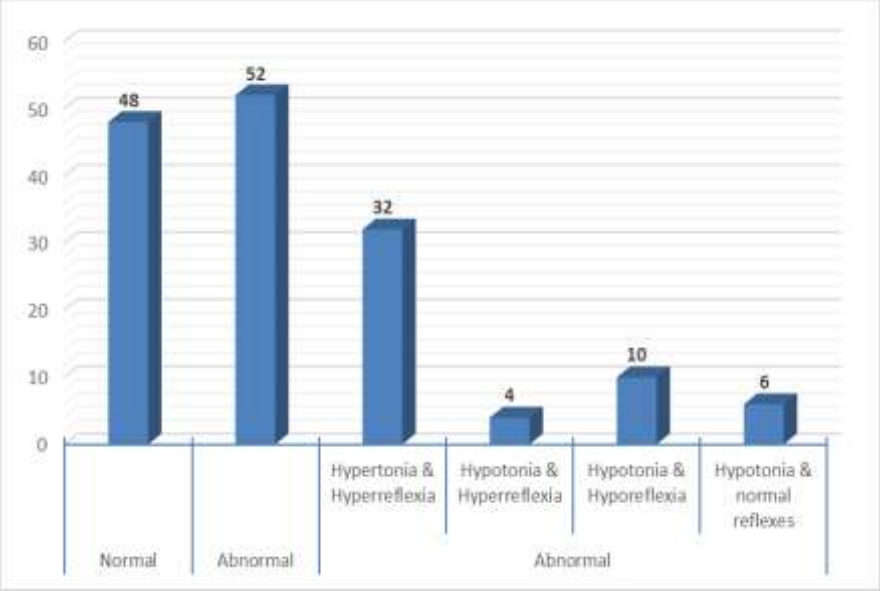

Fig. (1) Study group regarding Neurological examination.

4. Discussion

Epilepsy is a common neurological disorder that impacts approximately 3-6 out of every 1,000 children. It is important to note that 80% of individuals with epilepsy do not experience seizures, leading to a generally favorable prognosis. However, a subset of patients, comprising around 10-20%, endure medically intractable epilepsy, which significantly affects their quality of life [5].

The etiology of intractable epilepsy can differ based on factors such as age, geographic location, and, notably, the thoroughness of the investigative techniques used to determine the underlying cause of epilepsy. Several identified categories of etiology include epileptic encephalopathy, mesial temporal sclerosis, structural brain disease, and neurodegenerative disorders [6].

Several studies have aimed to identify risk factors associated with intractable epilepsy. Berg et al. focused on variables related to infantile intractable epilepsy, uncovering risk factors such as infantile spasms, age at seizure onset, distant symptomatic epilepsy, and a history of status epilepticus before the epilepsy diagnosis. In another study by Camfield et al., it was found that the absence of seizures in newborns, older age at seizure onset, normal IQ, and fewer than 20 seizures before starting medication were all significant predictors of remission [7].

Our study's findings regarding the age of symptom onset align with the research conducted by Sree and Belavadi (2020). They reported that among the cases, 15 individuals (50%) experienced symptom onset before the age of 1 year, while 8 individuals (26.6%) among the controls had a similar experience. Additionally, they observed that 15 cases (50%) and 22 controls (73.3%) developed seizures after the age of 1 year. Sree and Belavadi (2020) emphasized the significance of symptom onset before the age of 1 year in the cases, with a p-value of less than 0.001 [8].

In this study, we observed that 58% of patients with refractory epilepsy exhibited global developmental delay, while 68% of patients in the control group demonstrated normal development. The difference in developmental history between the research groups was found to be statistically significant. These findings are consistent with the results reported by Sree and Belavadi (2020), who found that 17 cases (33.3%) and 3 controls (10%) had a history of developmental delay, with a p-value of less than 0.001 [8].

5. Conclusions

Abnormal development, neuroimaging and frequent epileptiform discharges on EEG may indicate a higher likelihood of refractory epilepsy for further research with large number.

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