ORIGINAL ARTICLE

# Epidemiology of Epileptic Spasm and Affecting Factors on One-Year Prognosis: A Study in Tabriz Children's Hospital

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## ABSTRACT

**Objectives:** Epileptic Spasm (ES) is a special type of convulsive disorder that primarily occurs in infants, typically within the first year of life. This disorder is usually resistant to routine anticonvulsant drugs. This study aims to evaluate the epidemiology and factors affecting one-year prognosis in patients with ES in Tabriz Children's Hospital.

**Materials & Methods:** This descriptive-analytical cross-sectional study focused on patients diagnosed with ES who were referred to the neurology department of Tabriz Children's Hospital between 2015 and 2019. Data was collected using a census sampling method and a checklist that included demographic information and clinical and treatment histories. The results were then reported statistically.

**Results:** Thirty-seven patients were studied, with 15 (40.5%) exhibiting flexor seizures, eight (21.7%) extensor seizures, and 14 (37.8%) mixed seizures. The most common causes were prenatal insult (10 cases, 27.0%), cryptogenic (9 cases, 24.3%), and Central Nervous System (CNS) malformations (6 cases, 16.2%). Electroencephalography findings included modified hypsarrhythmia in 12 cases (30.8%), hypsarrhythmia in 16 (41.0%), and frequent epileptiform discharge in nine (23.1%). MRI and CT scans showed abnormalities in three cases (8.1%) and 16 cases (43.2%), respectively. Treatment involved Phenobarbital in 35 patients (94.6%), Vigabatrin in 29 (78.4%), and ACTH in 11 (29.7%). The one-year prognosis indicated 25 patients (67.6%) experienced disease recurrence, seven (18.9%) recovered with complications, and two (5.4%) died.

**Conclusion:** The most common causes of ES are prenatal insults, cryptogenic factors, and CNS malformations. The key one-year prognoses include disease recurrence and recovery with complications.

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## Introduction

Epileptic spasm (ES) is a unique type of convulsive condition that typically occurs in infancy, usually within the first year of life. These seizures often do not respond well to standard anticonvulsant medications. This disorder is commonly linked to developmental or intellectual disabilities and is characterized by a specific Electroencephalography (EEG) pattern called hypsarrhythmia, contributing to a distinct syndrome (1). Patients with this condition can be categorized into focal and diffuse groups, distinguished by differences in lateralization signs (2). The type of seizure experienced by these patients is determined by which group of muscles (flexor or extensor) is primarily

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affected. Flexor spasms are recognized mainly as seizures, with reports indicating that flexor spasms account for 42% of cases and flexor-extensor spasms for 50% of cases, making them some of the most commonly observed instances (1). ES typically manifests between the ages of three and eight months, with only 8% of cases occurring in individuals over the age of one year (3). The EEG of these patients exhibits a hypsarrhythmia pattern, characterized by slow waves and random spikes with high voltage (4, 5). Cases of ES are divided into cryptogenic and symptomatic groups. Cryptogenic spasms, which are rare, occur in newborns with normal birth and development at the time of the first seizure. On the other hand, prenatal and perinatal factors are often involved in the symptomatic spasms group (3, 6). ES can be caused by a variety of underlying diseases, which are categorized into three groups: prenatal, perinatal, and postnatal. Prenatal factors, accounting for 40% of cases, include Central Nervous System (CNS) malformations, chromosomal abnormalities, neurocutaneous syndromes, congenital CNS infections, and infants born with congenital metabolic disorders. Perinatal factors involve ischemic hypoxemic encephalopathy and hypoglycemia. Postnatal factors encompass brain infections, hypoxic-ischemic events, and brain tumors. In general, cortical malformations, hypoxic-ischemic events, and tuberous sclerosis are the most common causes of ES (4).

Regarding prognosis, nearly one-third of patients pass away after the age of three years, with 50% of them not surviving beyond the age of 10 years. Vision and hearing disorders have been observed in one-third to one-half of children with ES. Additionally, mental retardation has been reported in 71-90% of patients (1). Furthermore, evidence suggests a connection between long-term spasms and the effects on the disorder, as well as reduced growth and development of the nervous system (7). Currently, a lack of evidence exists regarding the effectiveness of medical and surgical treatments for improving long-term outcomes in patients with ES (8). Additionally, it has been observed that 25% of untreated children experienced spontaneous recovery of spasms and disappearance of hypsarrhythmia during the first year of life. However, overall, the impact on the growth and development of patients with ES is limited (4). No studies have been conducted on ES in our region, so given the risk of physical and neurological growth disorders in these patients, having information about their epidemiology and prognosis could lead to improvements in treatment processes. Therefore, this study aimed to investigate the epidemiology and influential factors in the one-year prognosis of patients with ES at the Tabriz Children's Educational and Therapeutic Center over the past five years.

# Materials &Methods

This research was a descriptive-analytical cross-sectional study, and its target population included all patients referred to the neurology department of Tabriz Children's Hospital in the last 5 years (2014-2018) who were diagnosed with ES by a specialist doctor.

Inclusion criteria comprise children with typical spasms and EEG results, including epileptiform changes. Exclusion criteria include patients with normal EEG results, patients with seizures without spasms, and inadequate clinical file information.

## Tools and techniques

A partially formalized survey was utilized to gather demographic information as well as the clinical and treatment background. The desired information was included age at first seizure (months), age at diagnosis (months), gender (boy- girl), type of seizure (flexor-extensor-mix), etiology (symptomatic-idiopathic), duration of hospitalization (days), neurological evaluation results, type of delivery (vaginal delivery-cesarean section), type of treatment and underlying diseases. Furthermore, the patient's parents were contacted to check the prognosis. After one year, the outcomes were assessed as either complete recovery, recovery with complications, or death.

## Statistical analysis

Data were analyzed using SPSS version 26 statistical software. The normality of the data was checked using the Kolmogorov-Smirnov test. Frequency (percentage) was used to describe qualitative data, and mean ± standard deviation was used for quantitative data if it was normal, and median if it was not normal. A p-value $<0.05$ was considered to be significant.

# Results

In this research, carried out on patients with ES referred to the Neurology Department of Tabriz Children's Hospital over the past five years (2014-2018), 37 patients were assessed. The median age of these patients was four (2-5.8) years. The majority of these patients were male, accounting for 23 cases (62.2%). Cesarean delivery was the most common type of delivery among the patients, with 21 cases (54.1%). A history of underlying disease was reported in 15 cases (40.5%) of the patients. Additionally, four cases (10.8%) and five cases (13.5%) of the disease were present in the parents and first-degree relatives of these patients, respectively (Table 1).

The distribution of seizure type and etiology characteristics in the subjects under study is presented in Table 2. As shown, the seizure type in the patients

was flexor in 15 cases (40.5%), extensor in eight cases (21.7%), and mixed in 14 cases (37.8%). The predominant etiology in the patients was prenatal insult in ten cases (27.0%), cryptogenic in nine cases (24.3%), and CNS malformation in six cases (16.2%).

Finally, the results pertaining to the hospitalization duration, diagnostic tools, medication type, and one-year prognosis in the subjects can be observed in Table 3. As shown, the median age at the time of diagnosis in these patients was five (3-6.8) months. Additionally, the median duration of hospitalization in the studied patients was 4.5 (3.7-3.8) days. The majority of the patients under study had a head circumference below five cm, accounting for 14 cases (37.8%). In the eye examination of these patients, one case (2.7%) had blindness, one case (2.7%) had a cherry-red spot, and one case (2.7%) had cataract. According to EEG findings in these patients, 12 cases (32.4%) had modified hypsarrhythmia, 16 cases (43.2%) had hypsarrhythmia, and ninr cases (24.3%) had frequent epileptiform discharge. Furthermore, based on the findings of Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) in these patients, abnormal findings were present in three cases (8.1%) and 16 cases (43.2%), respectively. The most commonly prescribed drugs in the studied patients were Phenobarbital in 35 cases (94.6%), Vigabatrin in 29 cases (78.4%), and ACTH in 11 cases (29.7%). The most frequently observed outcomes in the one-year prognosis of these patients were disease recurrence in 25 cases (67.6%), recovery with complications in seven cases (18.9%), and two cases (5.4%) of these patients passed away.

## Discussion

This research was carried out to explore the epidemiology and factors influencing the one-year outlook of patients with ES at Tabriz Children's Educational and Therapeutic Center, Iran. In this research, the prevalent seizure types among the patients under study were flexor seizures in 15 cases (40.5%), mixed seizures in 14 cases (37.8%), and extensor seizures in eight cases (21.7%). In 2017, Hussain et al. conducted a study involving 32 patients with ES who were admitted to medical centers in Baghdad. These patients were then monitored from January 2015 to January 2016 at the outpatient clinic of these hospitals. The patients' records were coded using their file and discharge card. The study design was descriptive and based on hospital data. The results revealed that 43.75% of patients experienced flexor spasms, 18.75% experienced extensor spasms, and 37.5% experienced flexor-extensor spasms (9). Taghdiri et al. carried out a detailed investigation involving 60 children, aged 2-24 months, who were diagnosed with ES and had been referred to the Pediatric Neurology Department of Mofid Childeren's Hospital between 1998 and2000. Among the clinical findings, 35 cases (58%) exhibited flexor type, six cases (10%) showed extensor type, and 19 cases (22%) displayed mixed type symptoms (10). In another study conducted by Taghdiri et al., they prospectively studied 30 children aged 2 to 24 months with ES who were referred to the Pediatric Neurology Department of Mofid Childeren's Hospital in Tehran, Iran, over a two-year period. The children were given Mogadon or Nitrazepam (NZP) at a dosage of 0.5-1 mg/kg/24h in three doses with food. After two, four, and six weeks of treatment, the patients were assessed for the cessation or reduction of seizures and any occurrence of side effects from the medication using relevant evaluation criteria. The study's findings indicated that 17 cases (57%) exhibited flexor-type clinical manifestations, two cases (3%) displayed extensor-type manifestations, and 11 cases (37%) showed mixed-type manifestations (11). The study by Mahjoob et al. revealed that the majority of clinical manifestations were associated with flexor movements, accounting for 45.5% (12). However, in Riikonen et al.'s study, involving a long-term follow-up of 214 children with ES syndrome, they concluded that the predominant clinical manifestations were related to mixed movements (13). The results obtained regarding the most common type of seizures in patients with epileptic spasm showed inconsistency compared to the study by Riikonen et al., who emphasized that most of the clinical manifestations are related to mixed types. However, the present study's findings were consistent with other studies that identified flexor movements as the most common clinical manifestation of this disease. The variance between this study and Riikonen's study could be attributed to several possible reasons, including differences in the target population and research environment, as well as variations in sample size and entry and exit criteria, such as disease severity and underlying factors.

Additionally, in this study, the most frequent etiology among the studied patients was prenatal insult in ten cases (27.0%), followed by cryptogenic in nine cases (24.3%), and CNS malformation in six cases (16.2%). The study by Nasirian, focusing on a 10-year investigation of infant spasm treatment at the Children's Medical Center, involved using baclonazepam, steroids, and a combination of both. This retrospective study utilized patient records, encompassing both outpatients and hospitalized individuals who received treatment. The results indicated that out of the 45 patients studied, the frequency of idiopathic etiology was 33%, while

symptomatic etiology accounted for 67% (14). In the study by Gibbs et al., involving 238 patients with ES, they concluded that the etiology of this disease is often idiopathic, accounting for 56%, followed by 44% being symptomatic (15). In their study, Ibrahim et al. included all patients with neonatal spasms who presented to Aga Khan University Hospital, Karachi, Pakistan, from January 2006 to April 2008. The inclusion criteria comprised clinical signs of neonatal spasm, hypsarrhythmia, or corrected hyperarrhythmia in EEG, and a follow-up period of at least six months. The type of drug distribution was randomized based on availability, cost, and ease of administration. The results indicated that 64.3% of cases were symptomatic, while 19.6% were cryptogenic, and 16.1% were idiopathic (16). In the study by Ladwig et al., the frequency of idiopathic etiology was 48%, while symptomatic etiology accounted for 52% of the 16 patients with ES (17). In the study by Jeavons et al., involving 150 patients with ES, they concluded that the majority of the etiology of this disease was symptomatic, representing 60%, with idiopathic etiology at 40% (18). According to the results obtained regarding the frequency of etiology in patients with ES, the present study exhibited inconsistency with the study by Gibbs et al., who indicated that most of the etiology of this disease is related to idiopathic causes. However, this study's findings were consistent with other studies that identified symptomatic etiology as the most common cause of this disease. The variance in the target population, research environment, sample size, and inclusion and exclusion criteria, such as the type and severity of the disease, as well as underlying factors, could explain why the results of this study were different from the study by Gibbs et al.

## In Conclusion

In this study, the most common types of seizures in the studied patients were flexor, mixed, and extensor, respectively. The most frequent etiologies in the studied patients were prenatal insult, cryptogenic, and CNS malformation, respectively. According to the EEG findings in these patients, the highest frequencies were associated with hypsarrhythmia, modified hypsarrhythmia, and frequent epileptiform discharge, respectively. The most prescribed drugs in the studied patients were Phenobarbital, Vigabatrin, and ACTH, respectively. The highest one-year prognosis in these patients was disease recurrence and recovery with complications, respectively.

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**Authors' Contribution**

Shahram Sadeghvand: Conceptualized and designed the study, provided overall supervision, and critically reviewed and approved the final manuscript. Ali Kamali: Collected the data, conducted statistical analysis, and drafted the initial version of the manuscript. Majid Mahallei: Conducted literature review, assisted with data analysis, and contributed to the writing of the discussion section. Shadi shiva: Coordinated data collection, ensured data accuracy and integrity, and contributed to drafting the methodology section. Gisou Erabi: Provided technical expertise, contributed to interpretation of the results, and assisted with manuscript revisions. Amirhosein Dadashzadeh Asl: Reviewed the manuscript critically for intellectual content, provided feedback, and contributed to the discussion and conclusion sections.

All authors have read and approved the final manuscript and agreed to be accountable for all aspects of the work.

**Conflicts of Interest**

The authors declare no conflicts of interest.

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