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What is the impact of etiology, lead time to treatment, and parental awareness on outcomes in infantile epileptic spasm syndrome?

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ABSTRACT

Objective: Infantile epileptic spasm syndrome (IESS) is a kind of developmental epileptic encephalopathy that can lead to severe outcomes, including drug-resistant epilepsy and impaired neurodevelopment. The underlying etiology, early diagnosis, and adequate treatment impact the outcome. Our study focused on examining the factors that influence the prognosis and the level of knowledge among families regarding IESS.
Methods: In the Department of Pediatric Neurology at Gazi University Hospital, we examined 62 IESS children's demographics, neuroimaging, metabolic and genetic findings, seizure characteristics, treatment choices, and long-term outcomes. Our study examined family awareness of seizures, lead time to treatment (LTT), and their impact on prognosis.
Results: Forty-two (67.8 %) patients presented with a symptomatic cause, with over half experiencing intraventricular hemorrhage and/or periventricular leukomalacia attributable to prematurity. The hormonal therapy (tetracosactide or oral prednisolone) was the preferred treatment. Treatment was effective for two-thirds of the patients. Nevertheless, hardly 50 % of the families acknowledged the "event" as a seizure. However, 34 (61 %) individuals had sought medical advice from a doctor during the first seven days. The mean time from the start of seizures to seeking medical care was 9.2 ± 5.7 days.
Conclusion: Our research revealed that the etiology was the most significant factor influencing the long-term outcomes of IESS. Additionally, we demonstrated that the clinicians who initially encountered the patients promptly referred them to pediatric neurology departments, despite the fact that the families' seizure awareness was poor. To help prevent this circumstance, it is important to provide information about infantile spasms to the families of high-risk infants.

1. Introduction

Infantile epileptic spasm syndrome is a kind of epilepsy that manifests itself mostly in the infant's first year of life and is marked by epileptic spasms. [1] The term "West syndrome" refers to the combination of epileptic spasms, hypsarthymia on an EEG, and neurodevelopmental delay. [2–4] IESS-related seizures that are referred to as "typical spasm seizures" might be confused with other diseases such as gastric reflux disease, colic, spasticity, benign sleep myoclonus, and frequent startles. [5,6] The diagnosis of IESS may take longer due to the difficulties in differentiating between "typical spasm seizures" and other diseases. Neurocognitive regression begins with seizures and sometimes even before seizures in the IESS; therefore, it is one of the conditions that must be treated immediately in pediatric neurology practice. Therefore, pediatricians and pediatric neurologists should be able to identify the distinctive seizures of infantile epileptic spasm. [7,8].

The prognosis for IESS is typically not favorable, especially in the long term. The prognosis of the condition is mostly based on its underlying etiology, although early and adequate treatment is also a critical element in improving results. [9–11] While the etiology is a non-modifiable issue, early detection of seizures and early and adequate treatment can improve the long-term prognosis of patients. [10,12].

The interval between the beginning of IESS seizures and the initiation of therapy by a pediatric neurologist might vary substantially across various countries and settings. The cause of this variation may be connected to the seizure knowledge level of families and clinicians, health policies, and access to health facilities. [8,9,12,13].

In our study, we aimed to analyze the clinical properties and

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diagnostic journey of IESS patients applied to the pediatric neurology clinic in a tertiary university hospital in Türkiye. The seizure awareness level of the families, the first recognition of the seizure, the first admission time to the pediatric neurology department, and the initiation of treatment and their relationship with the overall prognosis were examined.

2. Material and Methods

2.1. Patients Selection

In this retrospective study, we evaluated individuals diagnosed with IESS in the pediatric neurology department from January 2016 to December 2021, with a minimum of one year (12–84 months) of clinical follow-up.

2.2. Patients' data collection

By using the digital database, demographic information of the patients, complaints at presentation, seizure characteristics, presence of hypsarrhythmia in EEG, follow-up EEG data, neuroimaging findings, metabolic and genetic examination results, treatments applied, response to treatment, presence of epilepsy in follow-up, current treatments, and neurodevelopmental stages of the patient have been recorded.

2.3. Investigations

2.3.1. Neuroimaging

All patients had at least one cranial Magnetic Resonance Imaging (MRI) during follow-up. Both expert neuroradiologists and our pediatric neurology team assessed the patients' cranial MRIs.

2.3.2. Metabolic testing

All patients without structural abnormalities (congenital or acquired) underwent routine metabolic tests (serum ammonia, lactate, pyruvate, blood amino acids, urine organic acids, tandem mass spectroscopy, etc.) and, if required, advanced metabolic tests in consultation with the pediatric metabolism department.

2.3.3. Genetic testing

If no abnormalities were detected in the neuroimaging of the patients and there were no significant findings indicative of inherited metabolic diseases (such as positive results in metabolic tests and a family history of metabolic diseases), genetic evaluations were organized by genetic specialists, ranging from basic to advanced techniques (chromosome analysis, microarray, whole exome sequencing).

2.3.4. Etiology classification

Etiologies were classified into eight categories by the National Infantile Spasms Consortium (NISC): genetic, genetic-structural, structural-congenital, structural-acquired, metabolic, immune, infectious, and unknown. [14] Patients who have identifiable causes are often classified within the symptomatic etiology cohort. When metabolic, neuroimaging, and genetic analyses failed to identify the underlying etiology, those individuals were classified as having an unknown etiology.

2.3.5. Treatment protocol

In our clinic, steroid therapy (tetracosactide and oral prednisolone) was the initial treatment given to patients with IESS, excluding those with tuberous sclerosis. Owing to intermittently restricted access to tetracosactide in our country and familial concerns regarding steroid side effects, some patients were administered non-steroidal medications as the initial treatment.

2.3.6. Treatment response

Treatment response was determined as the cessation of spasm seizures after the first treatment (14–42 days) and the resolution of hypsarrhythmia in the EEG. [15–17].

2.3.7. Treatment lag definition and classification

We inquired with families to ascertain the duration required for patients to obtain treatment. These questions are given in the supplementary document. Treatment lag is defined as time in days from first epileptic spasm onset until first line treatment commencement.

2.3.8. Ethics

This study was approved by the Gazi University Medicine Faculty Ethics Committee.

2.4. Questionnaire

The researchers administered a questionnaire to the patients' families, either face-to-face or via telephone. During the questionnaire, we inquired with the families regarding their understanding of seizures, the child's current sleep pattern, and their involvement in daily activities appropriate for their age. We asked for the time of the first application to a doctor, the first department they applied to, the time of the first visit with a child neurologist, and the time of the antiseizure treatment initiation after the seizure onset. We have included our questionnaire form as a supplementary document.

2.5. Statistical analysis

We summarized the study results regarding the age at which epileptic spasms began, the time required to seek medical advice, and the lead time to treatment using the median, minimum, and maximum values from the distribution of continuous (numerical) variables. We summarized categorical variables using numbers and percentages. The numerical variables' normality was tested using Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling. The study compared categorical variables across groups using statistical tests. The Pearson Chi-Square test was used in 2x2 tables with predicted values of 5 or above. When predicted values were below 5, Fisher's Exact Test was used. The Fisher Freeman Halton test was also employed in RxC tables with predicted values below 5. For independent two-group comparisons of numerical variables without a normal distribution, the Mann-Whitney *U* test was used. In independent comparisons of more than two groups, the Kruskal-Wallis H test was used when numerical variables lacked a normal distribution. In nonparametric testing, the Dwass-Steel-Critchlow-Fligner test assessed group differences. A logistic regression analysis was conducted to identify the factors influencing the dependent variables, including the long-term outcome and presence of epilepsy, the relationship with etiology, treatment response, and lead time to treatment. Significance was assessed at $p < 0.01$ and $p < 0.05$ thresholds. All statistical analyses were performed using Jamovi (Version 2.3.24.0) and JASP (Version 0.17.1) with a 0.05 (p-value) significance level.

3. Results

3.1. Patients' characteristics

The demographic characteristics of the patients are detailed in Table 1.

A total of 62 children, 36 of whom were male, were diagnosed with infantile epileptic spasms. The age of patients ranged from one to twenty-two months, with a median age of 6.6 months ± 3.2 months. The ages of preterm infants were adjusted to reflect their corrected ages.

For each patient, seizure was their primary complaint. A total of nine patients who presented with premature birth, developmental delay, and hypotonia had been admitted to the pediatric neurology department for

Table 1
Patients' demographic characteristics.

	N(%)
Gender (M/F)	36/26 (58/42)
Age (median,month)	6.6 ± 3.2
Range(month)	1–22
Symptoms before seizures	5 (8)
Developmental delay	3 (13)
Hypotonia	2 (3)
Etiology	62 (100)
−Symptomatic	42(67.8)
−Unknown	20 (32.2)
Symptomatic etiology subgroups	
• Structural-acquired	22 (35.4)
PVL&ICH due to prematurity	14 (22.5)
Hypoxia-ischemic encephalopathy	6 (9,6)
Intracranial hemorrhagia&enfarct	2 (3.2)
• Metabolic diseases	9 (14.5)
• Genetic diseases	5 (8)
• Structrual-genetic (tuberous sclerosis)	4 (6.4)
• Structrual-congenital	2 ()(3.2)
Neuroimaging abnormality	
Yes	46 (74)
No	16 (26)
Spasm type	
Flexion	15 (24)
Extension	8 (13)
Mixed	39 (63)
First EEG	
Hypsarrhythmia	45 (73)
Atypical hypsarrhythmia	10 (16)
Hypsarrhythmia&Burst supression	7 (11)

Abbreviations: ICH: intracranial hemorrhage, PVL: periventricular leukomalacia.

evaluation before the seizure onset.

The patients' etiologies were categorized as genetic, genetic-structural, acquired structural, congenital structural, infectious, immune, or unknown. Structrual-acquired etiology is the biggest subset of the symptomatic group (n = 22, 35.4 %). In our study of the structural-acquired group, it was shown that "periventricular leukomalacia and/or intracranial hemorrhage due to prematurity" constituted the highest proportion (n = 14, 22.5 %). In this subgroup, the other ones had hypoxia-ischemic encephalopathy and cerebral haemorrhage or infarction.

The other etiologic reasons were metabolic, genetic, genetic-structural, and genetic-congenital diseases, in order of frequency. Twenty (32.2 %) individuals had an unknown etiology.

In all patients, cranial MRI was the preferred neuroimaging approach. Neuroimaging revealed abnormalities in 46 patients (74 %). Among these abnormalities, periventricular leukomalacia and cystic encephalomalacia owing to cerebral hemorrhages were the most prevalent (n = 14, 33.3 %). The cranial MRI of sixteen individuals did not reveal any abnormal abnormalities.

Upon suspicion of epileptic spasms in the patient following the family's admittance, a seizure video recording was conducted alongside an EEG. Our patients exhibited all three categories of seizures recognized in infantile epileptic spasm syndrome: flexion, extension, and mixed type involving both. 62 % mixed type, 13 % extension, and 24 % flexion spasms were observed, respectively.

The patients were monitored for a duration of two to seven years, with a median duration of three and a half years. Throughout the duration of the follow-up period, a total of 7 patients (11.3 %) were reported to have passed away.

3.2. EEG data

Experienced pediatric neurologists analyzed the EEG data of the patients. The initial EEG findings revealed that a total of 45 (73 %) exhibited hypsarrhythmia; 10 (16 %) displayed a combination of hypsarrhythmia and burst suppression pattern, while 7 (11 %) presented with atypical hypsarrhythmia.

The second EEG was conducted within a period of 14 to 42 days following the initial diagnosis. The findings of the second EEG indicated that 21(34 %) patients still had hypsarrhythmia.

3.3. Initial treatment and treatment response

Tetracosactide and oral prednisolone were the primary therapeutic options preferred by clinicians at rates of 31 (50 %) and 13 (21 %), respectively. The other treatments selected were vigabatrin, clobazam, and phenobarbital. (Fig. 1) Forty-one patients (66 %) exhibited a positive response to the initial treatment. (Fig. 2) Furthermore, the patients who positively reacted to treatment were diagnosed at a considerably older age compared to those who did not respond to treatment (p = 0.006). Table 2 illustrates the impact of hormonal and non-hormonal therapies on treatment efficacy.

3.4. Treatment lag

Families of twenty-nine patients (52.7 %) recognized the first seizure manifestation upon observing it in their child. Fifteen families (27.2 %) reported a lack of comprehension regarding the seizure event, yet they expressed concern that such an occurrence was abnormal for a child. Eleven families (20 %) initially perceived nothing peculiar about the incident; however, as the frequency of seizures escalated, they sought medical attention.

Following the emergence of complaints, 34 (61 %) families presentedto a physician within the initial 7 days (23 within the first 3 days), 12 (22 %) presented between 7 and 28 days, and the remaining 9 (16 %) families applied after 28 days. The average treatment lag was 9.2 days ± 5.7 days. (Fig. 3).

Patients with an unknown etiology sought medical help at a later stage compared to the symptomatic group. It was found that symptomatic cases were examined on days 0–3 more frequently than idiopathic cases, and idiopathic cases were examined on days 14–28 more frequently than symptomatic cases (p = 0.031).

A total of 45 families (81.8 %) sought the services of a pediatrician for the initial medical evaluation, while 6 families (12.7 %) consulted a pediatric neurologist, and 4 families (5.5 %) approached a family physician. Only four families brought up the fact that the doctor hadn't recognized the seizure at the first visit. The seizures were attributed to gas, colic, reflux, or jitteriness. Three of these physicians were general practitioners; one was a pediatrician. The average duration for these four families to seek a second medical opinion, following an initial doctor's failure to provide a diagnosis, was 11 days (5–17 days).

Patients referred to a pediatric neurologist were assessed at the corresponding department within an average of four days. Treatment was initiated within 0–3 days for the majority of cases (n = 52, 94.5 %), while a small proportion of patients (n = 2, 3.6 %) received treatment between 3–7 days after pediatric neurology examination. Only one patient (1.8 %) had a treatment initiation time exceeding seven days due to parental concerns.

3.5. Follow up period

In our cohort, 55 patients were under observation. Ten patients were monitored without medication after the spasms stopped. Out of the remaining patients, 20 received one or two antiseizure medications, while 25 were required to take two or more. In patients with symptomatic etiology, the frequency of seizures and seizure persistence during follow-up were significantly higher (p = 0.002 for each).

Medication-related side effects were observed in 30 patients (54.5 %). The largest group is those who used tetracosactide (n = 21). Among the side effects related to these medications, weight gain was observed in 15 (24.2 %), agitation in 13 (21 %), hair loss in 12 (19.4 %), and sleep

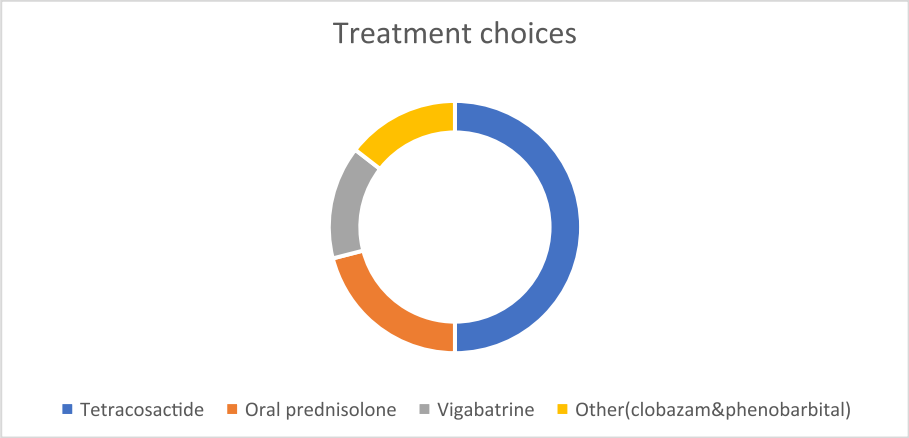


Fig. 1. Initial treatment choices.

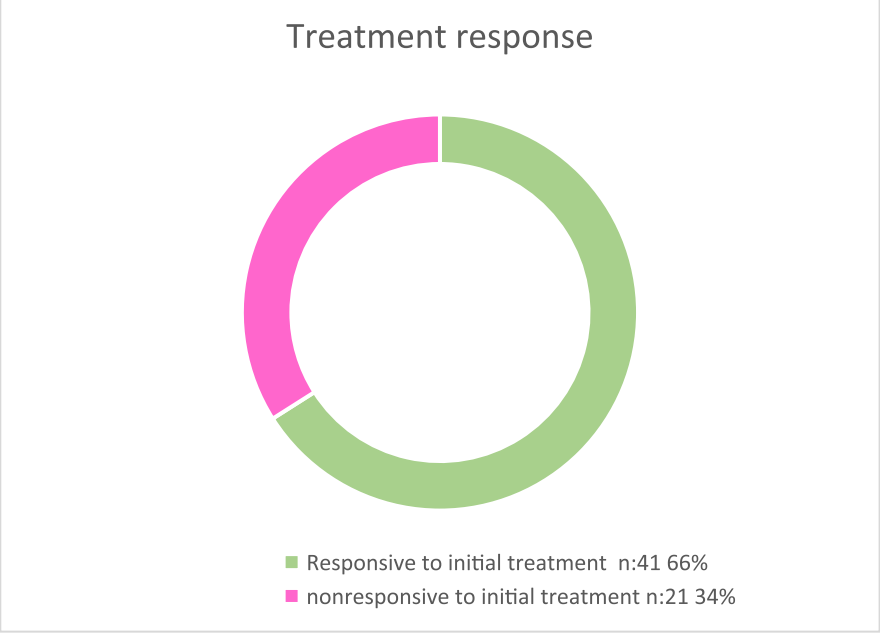


Fig. 2. Treatment respone to initial treatment.

Table 2
Relationship with treatment choice and response.

		Treatment response		
		Positive n (%)	Negative n (%)	Total n (%)
Treatment modality	Hormonal	31(50 %)	13(21 %)	44(71 %)
	Non-hormonal	10(16,1%)	8 (12,9%)	18(29 %)
				62(100 %)

problems in 2 (3.2 %) patients.

The psychomotor development of patients was evaluated during each examination conducted at our clinic. Neurodevelopmental outcomes were obtained through the acquisition of digital data and responses provided by the families of patients. In the assessment of psychomotor development, 41 (74.5 %) of 55 patients exhibited moderate to severe developmental delay, 9 (16.5 %) showed mild developmental delay, and 5 (9 %) showed normal development. The etiology, initial treatment, and the impact of treatment lag on intellectual development were also investigated. In our sample, it was determined that etiology significantly influenced long-term outcomes. The symptomatic group exhibited a higher prevalence of developmental delays ($p = 0.002$).

Based on the recent questionnaire provided by the families, it was found that 21 out of the patients (38 %) were capable of actively engaging in their daily routines and their own care. A total of eight patients (14.5 %) demonstrated the ability to engage in their daily activities at a level comparable to their peers. 13 patients (23.5 %) exhibited a mild-to-moderate delay in their ability to engage in daily activities compared to their peers. Patients with unknown etiology demonstrated a higher level of compatibility with their peers in terms of daily activities, whereas patients with symptomatic etiology exhibited significantly lower levels of participation in daily activities ($p = 0.002$).

The questionnaire concerning sleep quality identified inadequate sleep in 22 patients (40 %) as evidenced by the following: difficulty initiating sleep in 6 (9.7 % of cases), frequent awakenings in 17 (27.4 %), and brief sleep duration in 9 (14.5 %).

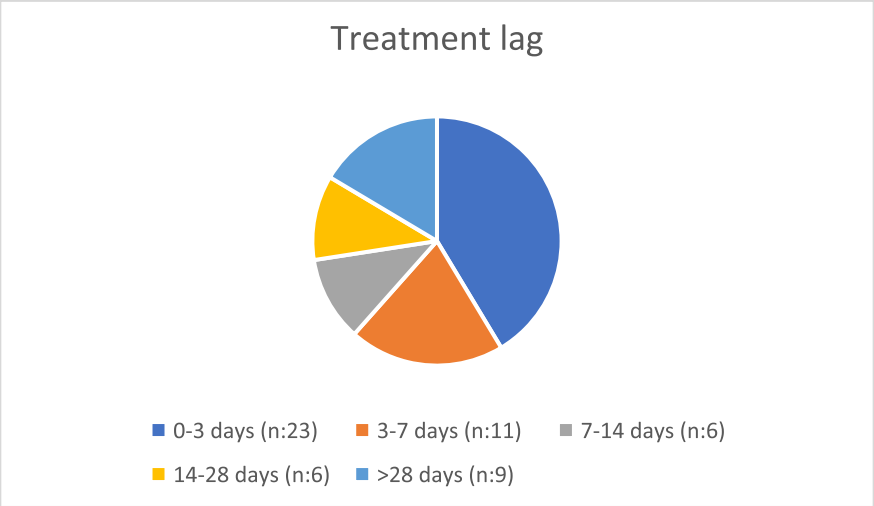


Fig. 3. Treatment lag distrubution.

4. Discussion

Our study included a retrospective analysis of 78 patients treated between 2016 and 2021 at a tertiary university hospital in Ankara, Türkiye. Excluding 16 patients due to discontinued follow-up, the study retrospectively assessed 62 patients and prospectively interviewed 55 families since 7 individuals died during the follow-up period. The average age at diagnosis was 6.6 ± 3.2 months, ranging from 1 to 22 months, and 33 (60 %) patients were male. Age at diagnosis and gender distribution in our study were comparable to those observed in previous studies. [5,18,19].

The etiology is the primary and unalterable element that significantly influences the long-term outcome of IESS. Identifying the cause is crucial for directing the treatment and predicting the outcome, as is the case in nearly all epileptic syndromes. [20,21] We assessed the patients' etiologies in two primary categories: symptomatic and unknown. Forty-two (68 %) patients belonged to the symptomatic etiology, whereas the remaining 20 (32 %) belonged to the group with an unknown etiology. Additionally, the symptomatic group was further examined in subcategories. These subgroups were structural-acquired, metabolic, genetic, structural-genetic, and structural-congenital etiologies. Similar subgroups were identified in the literature with regard to etiology. Unlike other studies that found a higher rate of Down syndrome and hypoxic ischemic encephalopathy, ours showed that the symptomatic group had a higher rate of intraventricular hemorrhage and periventricular leukomalacia due to prematurity. [5,10,18–24] The neonatal intensive care unit of our university hospital frequently monitors exceedingly and very premature infants, which may explain why premature infants comprised the majority of the symptomatic group in our study. Despite our small cohort, the higher prevalence of inherited metabolic diseases compared to the etiological studies reported in the literature can be attributed to the common occurrence of consanguineous marriage in our country. Alrifai et al. discovered comparable results in their study. [25].

All patients had cranial MRI as the recommended neuroimaging approach for etiological investigation. Nevertheless, even though not all cranial MRIs took place at our facility, both the pediatric radiology department and our own department evaluated them. Sixteen patients' (26 %) cranial MRIs did not reveal any abnormal findings. Twelve of these patients had an unknown etiology.

Our study included a long-term follow-up to assess prognosis and neurodevelopmental outcomes. During the follow-up, seven patients (11.3 %) passed away. None of the deceased patients died from problems arising from acute therapy. Due to the absence of a survey conducted among the relatives of these patients, complete death data for all patients could not be acquired. The data system revealed that two patients died of respiratory failure, while one patient passed away as a result of sepsis. While studies with follow-up periods of less than 10 years show comparable death rates, long-term studies reveal significantly higher rates, ranging from 17 % to 49 %. [23,26–29].

In the majority of patients (n = 55, 89 %), the initial EEG revealed hypsarrhythmia. The patients began receiving treatment the same day, or at the latest, the next day after the diagnosis. Second EEGs were obtained during the period of therapy from day 14 to day 42. Out of the 21 patients whose spasms and hypsarrhythmia pattern persisted on the second EEG, 8 were undergoing non-hormonal treatment. Treatment of these individuals was modified, and/or hormonal treatment was added.

Previous large-scale studies have consistently shown that hormonal treatments yield superior results compared to vigabatrin.[16,30,31] In our study, we preferred hormonal treatments (tetracosactide or oral prednisolone), accounting for 70 % of cases. Oral prednisolone was administered to patients who preferred not to have injections or for whom tetracosactide was not accessible.

Within our cohort, only fifty percent of the families were aware that what had occurred was a seizure. Although a quarter of the families were unaware of the seizure, they recognized its abnormality and sought medical attention. The remaining individuals only sought medical attention when the frequency of their seizures became unbearable. Hussain et al. similarly observed that families have a limited understanding of seizures. [32].

A significant proportion of patients (n = 46, 84 %) who exhibited a response to therapy sought medical consultation within the initial 28 days of seizure onset, with a majority (n = 34, 61 %) seeking medical attention within the first 7 days. The first doctor was mostly a pediatrician in our cohort (n = 45, 82 %). In this group, just one doctor was unaware that the patient was having a seizure. The first physician sought out by the families of seven patients was a pediatric neurologist. There were 6 patients in the pediatric neurology department who were being closely monitored due to prematurity, along with a patient with HIE. In our study, we found that nearly all of the pediatricians contacted by the families identified infantile spasms and directed the patient to the pediatric neurology department. A similar occurrence was seen in a prior study that assessed the knowledge, attitude, and practice (KAP) of pediatricians on IESS in our country. Yilmaz et al. found that pediatricians had an adequate level of KAP regarding IESS. Also, this study revealed that most of the pediatricians had knowledge regarding the accurate diagnostic tools for infantile spasm as well as the appropriate treatment. However, they expressed their intention to refer the patient for a final

diagnosis, treatment, and follow-up due to the comparatively easier accessibility of a pediatric neurologist, as compared to many other countries. [33] The time interval between patients' initial consultation with a physician and their subsequent evaluation by a pediatric neurologist is limited to a maximum of seven days. The predominance of state hospitals and university hospitals in our country's healthcare system has made it easier to get prompt and convenient access to a pediatric neurologist. In our country, individuals have convenient and prompt access to pediatricians and speedy referral to specialized pediatric departments, surpassing the accessibility provided in several other countries, without incurring any extra fees. [5,7,8,19,22,32,34].

Research on IESS has thoroughly investigated the time interval between the beginning of spasms and the initiation of therapy, known as the lead time to treatment (LTT). The general consensus is that a treatment lag of more than one week is considered long, even though there is disagreement over the number of days that define "this period" as long or delayed. [12] Based on a review of the relevant literature, it was determined that two studies—authored by Lagae et al. and Auvin et al.—documented the shortest LTT as 6 and 10 days, respectively. Hussain et al. reported an average of 24.5 days, whereas Cohen et al. reported an average of 25 days. [8,9,32,35] Other studies have determined that the LTT is at least four weeks. [5,7,13,22,36–38] The mean LTT in our research was 9.2 days (range: 1–64 days), with a median time of 5 days. The median time was found to be shorter than the mean time because the largest group consisted of patients admitted within the first seven days.

Several reasons contribute to the delay in treatment. Factors including misdiagnosis, familial dynamics, referral systems, and health policies may contribute to the current situation. The primary cause of this delay in developed countries typically stems from the difficulties of the referral system and/or the challenges of health insurance. [7,32] In developing countries, the delay may be attributed to seeking medical attention late or difficulty accessing initial therapies. [19,22,34] Furthermore, misdiagnosis and the scarcity of pediatric neurologists may contribute to treatment delays. The most common initial diagnoses by physicians are gastric reflux, colic, sleep myoclonus, and typical infant behaviors. [8] The "Infantile Spasm Action Network" (ISAN), has emphasized the significance of prompt and precise diagnosis. [6] The study conducted by Rao et al. shows that the extensive integration of technology into everyday life has been beneficial in accurately diagnosing patients through the use of smartphone-recorded videos. [39] By enhancing societal and healthcare professionals' awareness, the aim is to reduce the interval between the onset of spasms and the administration of medication for patients.

The destructive effects of infantile spasms on the neurological system are well established. Numerous studies have been conducted to investigate the consequences of IIES, with a particular focus on long-term outcomes and the determinants that impact them (e.g., etiology, treatment alternatives, lead time to treatment). Multiple studies have consistently demonstrated that individuals with idiopathic patients exhibit a more favorable prognosis when compared to those in the symptomatic group. [10,36,40–42] Our study revealed that the idiopathic group had a superior treatment response and long-term prognosis compared to the symptomatic group. Literature-based research has established that hormonal alternatives, particularly tetracosactide, should be the treatment of choice for all patients, irrespective of their etiology (with the exception of tuberous sclerosis). [17,42–45] Our initial treatment approach involved utilizing hormonal treatments, which were selected based on a combination of up-to-date literature and practical considerations. Many studies showed that LTT was strongly linked to neurodevelopmental outcomes and epilepsy in the future. [10,12,13,35,41,46] This relationship could not be established in a limited number of studies. [36,38,47] We hypothesized in the beginning of our study that the impact of LTT on long-term outcomes would be favorable. Early LTT (<7 days) was associated with a more favorable treatment response, according to our study; however, its impact on long-term outcomes could not be established. Out of the 34 patients who applied within the first 7 days, only 20 % (n = 7) did not exhibit neurodevelopmental delay or epilepsy. Our findings indicate that individuals in the symptomatic group had a worse outcome, even when subjected to short-term (<7 days) LTT. Despite the brevity of LTT in our study, its impact on prognosis did not align with the findings in the existing literature. There are other factors contributing to this predicament. The spasms may have begun prior to the families' awareness, and the majority of the patients belong to the symptomatic category, which suggests a poor prognosis.

A significant proportion of the whole patient population, 74.5 %, had neurodevelopmental impairment. In accordance with their age, patients' participation in daily activities was quite low (n = 21, 38 %). Neurodevelopmental delay, similar to our study, was commonly found in studies that looked at the long-term outcome. [5,10,12,37,41,47].

Our study has several limitations. Due to the retrospective nature of the study, variations in etiological groups were observed, and the determination of drug preferences rested with the attending physician. Moreover, our cohort comprised a small group. Studies with larger patient populations and prospective designs will answer more questions on treatment effects.

5. Conclusion

Despite the small patient population, it may be inferred from the data that early intervention for hypsarrhythmia and spasms (within 7 days) is associated with a positive response to therapy. Still, epilepsy development and cognitive outcome may be more closely linked to etiology. At the same time, we demonstrated that even though the families had a low level of awareness regarding seizures, the physicians who initially examined the kids were quick to refer them to pediatric neurology departments. Making sure that families of babies who are at risk are aware of IESS is of the utmost importance. Notwithstanding the inherent constraints, our study findings underscore the need for timely and accurate management of hypsarrhythmia and spasms, as this is the domain in which physicians may exert the most influence on prognostic outcomes.

Authors contribution

Study conception and design: D.M. Author and E.A Author; data collection: D.M. Author; analysis and interpretation of results: E.S. Author, D.M. Author, T.H. Author; draft manuscript preparation: E.S Author, D.M. Author, A.S. Author, E.A. Author All authors reviewed the results and approved the final version of the manuscript.

CRediT authorship contribution statement

Deniz Menderes: Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation. **Esra Serdaroğlu:** Writing – review & editing, Visualization, Supervision, Project administration, Methodology, Investigation. **Tuğba Hırfanoğlu:** Supervision, Resources, Data curation. **Ayşe Serdaroğlu:** Supervision. **Ebru Arhan:** Validation, Supervision, Methodology, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2024.110178.

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