ORIGINAL ARTICLE

Electroclinical Profiles of Children with Electrical Status Epilepticus: Insights From Tertiary Care Centre

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Pak Pediatr J 2025; **49(3&4):** 263-69

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Received for publication 10-08-2025;
Revised accepted 27-10-2025

How to cite this: Anjum N, Zafar F, Yousuf M, Safdar, Rehman ZUr, Tariq A
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Pak pediatr j. 2025; 49(3&4): 255-61

ABSTRACT

Objective: This study aimed to delineate the electroclinical spectrum of children diagnosed with Electrical Status Epilepticus (ESE) in a tertiary center in Pakistan.

Study Design: Retrospective cross-sectional descriptive observational study.

Place and Duration of Study: Department of Pediatric Neurology, The Children's Hospital and Institute of Child Health, Multan, conducted between January 2020 and December 2024.

Material and Methods: A total of 127 pediatric patients with EEG-confirmed ESE were retrospectively reviewed. Clinical characteristics, seizure semiology, electroencephalographic findings, and treatment strategies were analyzed. Data were entered and processed using SPSS version 25.

Results: Of the 127 patients, 66.9% (n=85) were male, with a mean age at diagnosis of 6.9 years (±3.3). Seizures occurred daily in more than half (54.3%, n=69). Generalized tonic–clonic seizures were the predominant type (50.4%, n=64), followed by myoclonic (22.0%, n=28) and focal tonic–clonic seizures (18.1%, n=23). The average diagnostic delay was 2.75 years. Developmental delay was present in 67.7% (n=86), while regression was documented in 8.7% (n=11). EEG revealed generalized ESE in 84.3% (n=107), focal involvement in 10.2% (n=13), and multifocal abnormalities in 5.5% (n=7). The commonest etiologies included idiopathic epilepsy (41.7%), developmental and epileptic encephalopathies (28.3%), and cerebral palsy with epilepsy (13.4%). Sodium valproate was the most frequently prescribed drug, either as monotherapy or in polytherapy, with polytherapy required in more than half of the cases (53.5%).

Conclusion: ESE is associated with substantial diagnostic delays and considerable neurodevelopmental compromise in Pakistani children. Early recognition and individualized therapeutic strategies are critical to improving outcomes.

Key Words: Electrical status epilepticus, Pediatric epilepsy, EEG

INTRODUCTION

Epilepsy remains one of the most prevalent chronic neurological disorders worldwide, affecting nearly 70 million individuals, with childhood constituting a particularly vulnerable period due to its profound impact on cognition, language, and psychosocial development.[1]

Electrical Status Epilepticus (ESE) — also referred to as Electrical Status Epilepticus in slow wave Sleep (ESES) — represents a rare yet severe epileptic encephalopathy, occurring in approximately 0.2–0.5% of children with epilepsy. It is characterized by near-continuous epileptiform discharges during non-rapid eye movement (NREM) sleep, leading to progressive neurocognitive impairment and language regression, and is frequently associated with Encephalopathy with Continuous Spike-and-Wave during Sleep (CSWS) and Landau – Kleffner Syndrome (LKS).[2]

The defining electroencephalographic hallmark of ESE is a spike - wave index (SWI) exceeding 85%, calculated as: SWI (%) = (Duration of Spike-Wave Activity ÷ Total NREM Sleep Time) × 100.[3]

Although this criterion has been widely used, growing evidence indicates that significant cognitive and behavioral decline can also occur at intermediate SWI thresholds (50–85%), raising questions about rigid diagnostic cut-offs.[4] This is particularly relevant in low- and middle-income countries (LMICs) such as Pakistan, where prolonged overnight EEG monitoring — considered the diagnostic gold standard — is not routinely accessible.[5] Sleep-deprived or limited EEG protocols are often employed as substitutes, but their sensitivity remains suboptimal, and the lack of standardized guidelines complicates interpretation.[6]

The consequences of untreated or delayed recognition of ESE are profound. Studies have documented irreversible declines in IQ scores, with losses of up to 30 points, along with lasting impairments in executive function, working memory, and expressive language skills, even in children whose seizures eventually remit.[7] This neurocognitive damage is thought to result from persistent epileptiform discharges disrupting thalamocortical networks, which are critical for synaptic plasticity, language acquisition, and memory consolidation during early development.[8] Importantly, a delay of more than 1–2 years in treatment initiation often results in permanent deficits, underscoring the importance of timely detection.[9]

Widely used anti-seizure medications such as valproate and levetiracetam yield satisfactory seizure control in only 40–60% of cases.[10] Corticosteroids and immunotherapies demonstrate greater efficacy in reducing EEG abnormalities, yet their side-effect profiles, including weight gain, mood disturbances, and metabolic complications, limit long-term use.[11] Non-pharmacological approaches such as ketogenic diet and vagus nerve stimulation have shown promise in refractory cases but remain underutilized in resource-limited contexts.[12] A further complexity lies in the observation that normalization of EEG does not always correlate with cognitive recovery, reflecting the dual need to address both seizure suppression and neurodevelopmental rehabilitation.[13]

Most available data on ESE emanate from high-income countries, leaving a significant gap in understanding its epidemiology and management in LMICs, where pediatric epilepsy carries a disproportionate burden.[14] In Pakistan, delays in ESE diagnosis frequently exceed two years, largely due to limited access to pediatric neurologists, inadequate EEG facilities, and sociocultural stigma surrounding epilepsy.[15] Consequently, children often present with advanced neurodevelopmental impairment at the time of diagnosis.

The current study aims to present a comprehensive electroclinical and therapeutic profile of children with ESE managed at a tertiary care hospital in Multan, Pakistan. By documenting the seizure types, EEG features, developmental status, treatment regimens, and etiological spectrum.

MATERIAL AND METHODS

This retrospective cross-sectional descriptive observational study was carried out in the Department of Pediatric Neurology, The Children's Hospital and Institute of Child Health (CH&ICH), Multan, covering the period from January 2020 to December 2024. Approval for the study was granted by the Institutional Review Board (CH\&ICH/ERC/2025/007). Given the retrospective nature, the requirement for informed consent was waived, though strict confidentiality was ensured.

Children aged 1 to 15 years with an EEG-confirmed diagnosis of Electrical Status Epilepticus (ESE) were included. Cases with incomplete EEG data or those presenting with convulsive/non-convulsive status epilepticus unrelated to ESE were excluded.

Clinical and demographic details including age, sex, semiology, treatment strategies, developmental milestones, family history, and etiology were retrieved from hospital records. EEGs were reviewed by a pediatric neurologist.

Data were analyzed using SPSS version 25.0, with descriptive statistics applied to summarize clinical and electroencephalographic profiles.

RESULTS

A total of 127 children were identified with a confirmed diagnosis of Electrical Status Epilepticus (ESE) during the study period. Demographic and clinical characteristics are summarized in **table 1,** which outlines sex distribution, development status, seizure classification, and treatment modalities among the studied cohort. There was a clear male predominance, with 85 boys (66.9%) and 42 girls (33.1%), yielding a male-to-female ratio of approximately 2:1. The mean age at diagnosis was 6.96 ± 3.32 years, and while the youngest child was diagnosed at one year of age, the oldest was fifteen years. A positive family history of epilepsy was reported in 31 children (24.4%).

More than half of the children (54.3%, n=69) experienced daily seizures, significantly disrupting daily functioning, education, and social interaction. Another 44.9% (n=57) reported seizures occurring on a monthly basis, while only a minority presented with less frequent episodes. The most common seizure type was generalized tonic – clonic seizures (GTCS), recorded in 64 patients (50.4%). This was followed by myoclonic seizures in 28 children (22.0%), focal tonic – clonic seizures in 23 patients (18.1%), and a mixed pattern of generalized tonic – clonic seizures with myoclonic jerks in 11 children (8.7%). The mean interval from seizure onset to formal diagnosis was 2.75 ± 2.86 years (median 1.5 years, IQR 0 15 years). The distribution of EEG findings is depicted in **fig 1,** while **fig 2** is the representative EEG epoch of a patient with ESE showing a spike wave index (SWI) of 85%.

Of the total, 67.7% (n=86) demonstrated global developmental delay, with varying degrees of language, motor, and cognitive deficits. In addition, developmental regression was identified in 11 children (8.7%), representing those who had initially achieved age-appropriate milestones but subsequently lost previously acquired skills such as speech, vocabulary, or social responsiveness. Only 23.6% (n=30) maintained age-appropriate development, emphasizing the pervasive neurocognitive burden associated with ESE.

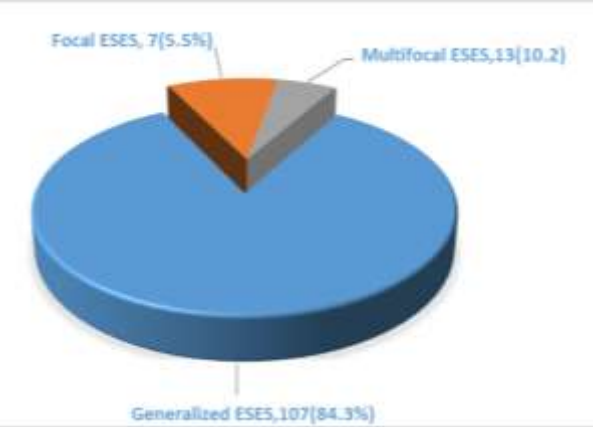

Fig 1: **Profile of EEG findings**

TABLE 1: Demographic, clinical, seizure, and treatment characteristics of pediatric ESE (N = 127)

Parameter	Number of Patients (n)	Percentage
• Male	85	66.9
• Female	42	33.1
• Developmental Delay	86	67.7
• Developmental Regression	11	8.7
Epilepsy in family member	31	24.4
Seizure classification		
• Generalized Tonic-Clonic	64	50.4
• Focal Tonic-Clonic	23	18.1
• Myoclonic Seizures	28	22.0
Treatment Modalities		
• Valproate Monotherapy	22	17.3
• Polytherapy	68	53.5
• No Antiepileptic Drugs	24	18.9

The majority of children (84.3%, n=107) exhibited generalized ESE. Focal ESE was documented in 13 patients (10.2%), typically involving the frontal or centro-temporal regions. A smaller proportion, 7 children (5.5%), showed multifocal ESE, with discharges arising from multiple cortical regions simultaneously. The dominance of generalized patterns in this cohort may reflect delayed

presentation, by which time focal discharges may have already evolved into generalized activity.

Idiopathic epilepsy was the most frequent etiology, accounting for 41.7% (n=53). Developmental and epileptic encephalopathies were identified in 28.3% (n=36), representing children with genetic or structural brain abnormalities leading to intractable seizures and global developmental impairment. Cerebral palsy with associated epilepsy accounted for 13.4% (n=17). Less common causes included mitochondrial disorders such as MELAS (0.8%, n=1), Rasmussen's encephalitis (0.8%, n=1), and metabolic encephalopathies (1.6%, n=2).

Fig 2: One epoch of EEG of suggestive of ESE

Notably, 24 patients (18.9%) were not receiving any anti-seizure medications at the time of review, largely attributable to delayed diagnosis, parental reluctance, or socioeconomic constraints. Among those who received treatment, monotherapy was prescribed in 27.6% (n=35). The most commonly prescribed single agent was sodium valproate (17.3%, n=22), reflecting its wide availability, cost-effectiveness, and broad-spectrum efficacy. Levetiracetam was the next most frequent monotherapy (7.9%, n=10). However, the majority of patients (53.5%, n=68) required polytherapy. The most frequent two-drug combinations were valproate with levetiracetam (7.1%, n=9), valproate with carbamazepine (6.3%, n=8), and valproate with clobazam (4.7%, n=6). More complex regimens involving three or more agents were necessary in 16 patients (12.6%). Overall, valproate was used in 63.8% of all treatment regimens, while levetiracetam was prescribed in 41.7%, either as monotherapy or in combination.

DISCUSSION

Electrical Status Epilepticus (ESE) represents one of the most disabling pediatric epilepsy syndromes due to its dual impact on seizures and neurodevelopment. The present study, based on five years of experience at a tertiary care centre in Multan, Pakistan, provides important insights into the electroclinical spectrum, treatment patterns, and challenges in managing this rare condition in a resource-constrained environment. Our findings demonstrate a male predominance, a high burden of generalized tonic–clonic seizures, substantial diagnostic delays, and significant neurodevelopmental compromise. These results are broadly in line with global observations, though several aspects highlight the specific barriers and practice realities within low- and middle-income countries (LMICs).

In this cohort, generalized tonic–clonic seizures were the most frequent seizure type, affecting half of the children. This is consistent with the reports of Jain et al. and Kramer et al., who also observed generalized seizures as the predominant clinical manifestation in ESE cohorts.[16] The prominence of generalized seizures reflects the diffuse cortical excitability characteristic of the condition. The presence of myoclonic and focal tonic–clonic seizures in nearly 40% of patients, however, underscores the heterogeneity of seizure semiology in ESE, consistent with earlier reports by Fernández and colleagues.[17] Such diversity in presentation often complicates recognition, particularly in LMICs where detailed seizure documentation and video-EEG monitoring are not readily available.

The diagnostic delay in our cohort averaged nearly three years, which is concerning given that persistent epileptiform discharges during sleep can rapidly and irreversibly impair cognition.[18] Previous studies have indicated that delays beyond one to two years are strongly associated with poorer long-term neurocognitive outcomes, particularly in language acquisition and executive function.[19] In Pakistan, as in other LMICs, such delays are attributable not only to limited access to pediatric neurologists and EEG facilities but also to sociocultural stigma that discourages early medical consultation. This highlights an urgent need for targeted awareness programs and

improved referral systems for children with suspected epilepsy.

The most striking finding in our study was the high prevalence of developmental impairment: two-thirds of children presented with global developmental delay, and nearly 9% exhibited frank developmental regression. This aligns with Hughes and colleagues, who emphasized that continuous epileptiform activity is strongly correlated with regression in language and cognition.[20] In our series, only one in four children achieved age-appropriate milestones, underscoring the devastating neurocognitive burden associated with ESE.

The predominance of generalized EEG abnormalities (84.3%) in our cohort likely accounts for the widespread deficits observed, as generalized discharges are known to disrupt multiple neurocognitive domains simultaneously.[21] Children with focal ESE (10.2%) and multifocal patterns (5.5%) represented smaller subgroups but are clinically important, as earlier studies have shown that focal discharges may cause selective impairments, particularly in expressive language, whereas multifocal abnormalities are linked with diffuse and often more severe impairment.[22] These findings suggest that detailed EEG characterization has prognostic value, not only in confirming the diagnosis but also in anticipating the type and severity of neurodevelopmental consequences.

The etiological profile in this study was heterogeneous, with idiopathic epilepsy being the most common cause, followed by developmental and epileptic encephalopathies and cerebral palsy with epilepsy. This distribution mirrors findings from other regions, although structural causes such as cerebral palsy may be more prominent in LMICs due to higher rates of perinatal brain injury.[23] The presence of mitochondrial disorders (e.g., MELAS), Rasmussen's encephalitis, and metabolic encephalopathies, albeit rare in this series, reflects the broad etiological spectrum of ESE and emphasizes the importance of considering genetic and metabolic investigations in children with atypical presentations. Unfortunately, such advanced testing remains limited in Pakistan, contributing to diagnostic uncertainty in many cases.

Sodium valproate was the cornerstone drug, used either as monotherapy or as part of multidrug regimens in nearly two-thirds of patients. However, previous studies, including those by Fejerman and Raha et al., have shown that valproate alone rarely normalizes EEG activity or reverses cognitive decline.[24] This explains why more than half of our patients ultimately required polytherapy, often combining valproate with levetiracetam, carbamazepine, or clobazam.

Beyond conventional anti-seizure medications, immunomodulatory therapies such as corticosteroids and intravenous immunoglobulin (IVIG) have demonstrated efficacy in reducing epileptiform discharges and improving cognition in selected children with ESE. Han et al. reported significant benefits with high-dose corticosteroids, while other studies have noted improvement with IVIG.[24] However, such therapies were not widely utilized in our setting due to cost, limited availability, and concerns about side effects. Non-pharmacological options such as ketogenic diet therapy and vagus nerve stimulation have also been reported in international cohorts but remain inaccessible to most patients in Pakistan.

Furthermore, as Specchio and Arzimanoglou have emphasized, the integration of precision medicine, including genetic testing and advanced neuroimaging, holds promise for tailoring treatment.[25]

Our findings underscore several urgent priorities. First, reducing diagnostic delays must be a central focus. This requires expanding access to EEG services, training pediatricians to recognize red flags such as language regression and nocturnal seizures, and establishing clear referral pathways to specialized epilepsy centres. Second, treatment strategies must be individualized, balancing efficacy with tolerability, and incorporating caregiver education to enhance adherence. Third, there is a need for national guidelines for the management of ESE in Pakistan, reflecting both international evidence and local realities. Finally, investment in genetic and metabolic testing, as well as non-pharmacological therapies, is essential to provide comprehensive care.

CONCLUSION

This study provides one of the most comprehensive descriptions of the electroclinical features and treatment patterns of children with Electrical Status Epilepticus (ESE) from a tertiary care centre in Pakistan. To improve outcomes, it is imperative to enhance early recognition and the study reinforces the urgent need for national strategies and policy interventions to bridge the epilepsy treatment gap in Pakistan and similar resource-limited settings.

Acknowledgment: The authors wish to acknowledge Mr. Javed Ansari, EEG Technologist, at the Children's Hospital Multan, for his valuable technical assistance in EEG data acquisition.

Source of funding: None
Conflict of interest: None

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REFERENCES

1. Waris A, Siraj M, Khan AA, Lin J, Asim M, Alhumaydhi FA. A Comprehensive Overview of the Current Status and Advancements in Various Treatment Strategies against Epilepsy. ACS Pharmacol Transl Sci. 2024. https://doi.org/10.1021/acsptsci.4c00494
2. Fernández IS, Peters J, Takeoka M, Rotenberg A, Prabhu S, Gregas M, et al. Clinical features of electrical status epilepticus in sleep irrespective of focal or generalized EEG activation. J Child Neurol. 2013;28 (1):83-9. doi:10.1177/0883073812440507.
3. Wu T, Avidan AY, Engel J Jr. Sleep and epilepsy: clinical spectrum and updated review. Sleep Med Clin. 2021; 16(2): 389-408. doi:10.1016/j.jsmc.2021.02.011.
4. Bonardi CM, Mignot C, Serratosa JM, Giraldez BG, Moretti R, Rudolf G, et al. Expanding the spectrum of CNKSR2-related encephalopathy with status epilepticus during sleep. Clin Neurophysiol. 2020;131 (5):1030-9. doi:10.1016/j.clinph.2020.01.020.
5. Lu G, Cheng Y, Wang Y, Hu J, Zhang F, Li W, et al. Prevalence and risk factors of electrical status epilepticus during slow-wave sleep in self-limited epilepsy with centrotemporal spikes. Clin EEG Neurosci. 2024; 55 (2): 265-71. doi:10.1177/15500594231182758.
6. Pack AM. Epilepsy: overview and revised classification of seizures and epilepsies. Continuum (Minneap Minn). 2019;25 (2):306-21. doi:10.1212/CON.0000000000000707.
7. Kessi M, Peng J, Yang L, Xiong J, Duan H, Pang N, et al. Genetic causes of electrical status epilepticus during slow-wave sleep: a systematic review. BMC Genet. 2018;19(1):40. doi:10.1186/s12863-018-0628-5.
8. Cantalupo G, Pavlidis E, Beniczky S, Avanzini P, Gardella E, Larsson PG. Quantitative EEG in encephalopathy related to status epilepticus during slow sleep. Epileptic Disord. 2019;21(S1):31-40. doi:10.1684/epd.2019.1055.
9. Chapman KE, Haubenberger D, Jen E, et al. Unmet Needs in Epileptic Encephalopathy With Spike-and-Wave Activation in Sleep: A Systematic Review. *Epilepsy Research*.December 2023. DOI: 10.1016/j.eplepsyres.2023.107278.
10. 10.Kholin AA, Zavadenko NN, Fedonyuk ID, Il`ina ES. Efficacy and safety of levetiracetam in children with electrical status epilepticus during slow-wave sleep (eses). Epilepsia and paroxyzmal conditions. 2017 Aug 29;9(2):21–8.
11. Sánchez Fernández I, Hadjiloizou S, Eksioglu Y, Peters JM, Takeoka M, Tas E, et al. Diazepam responsiveness of sleep-potentiated spiking in electrical status epilepticus during sleep. Pediatr

Neurol. 2012; 46(5): 312-8. doi:10.1016/j.pediatrneurol.2012.02.017.

12. Kramer U, Sagi L, Goldberg-Stern H, Zelnik N, Nissenkorn A, Ben-Zeev B. Clinical features and treatment of children with electrical status epilepticus in sleep. Epilepsia. 2009;50(6):1517-24. doi:10.1111/j.1528-1167.2008.01891.x.
13. Nickels K, Wirrell E. Electrical status epilepticus in sleep. Semin Pediatr Neurol. 2008;15(2):50-60. doi:10.1016/j.spen.2008.03.002.
14. McVicar KA, Shinnar S. Landau-Kleffner syndrome, ESES, and childhood language regression. Ment Retard Dev Disabil Res Rev. 2004;10(2):144-9. doi:10.1002/mrdd.20028.
15. Van Hirtum-Das M, Licht EA, Koh S, Wu JY, Shields WD, Sankar R. Variability of electrical status epilepticus in sleep in children. Epilepsy Res. 2006;70 Suppl 1\:S248-58. doi:10.1016/j.eplepsyres.2006.01.020.
16. Jain P, Sharma S, Tripathi M. Epileptic encephalopathies in children: diagnosis and management. Epilepsy Res Treat. 2013;2013:501981. doi:10.1155/2013/501981.
17. Hughes JR. Landau-Kleffner syndrome, ESES, and continuous spike-wave sleep: a review. Epilepsy Behav. 2011;20(2):247-53. doi:10.1016/j.yebeh.2010.10.015.
18. Fortini S, Corredera L, Pastrana AL, Reyes G, Fasulo L, Caraballo RH. Hemi-ESES or hemi-continuous spikes during slow sleep: study of 21 cases. Seizure. 2013;22(7):565-71. doi:10.1016/j.seizure.2013.04.006.
19. Kotagal P. Treatment approaches for electrical status epilepticus in slow-wave sleep. Epilepsy Curr. 2017;17(4):214-6. doi:10.5698/1535-7597.17.4.214.
20. Raha S, Shah U, Udani V. Neurocognitive and behavioral impairments in ESES and related syndromes. Epilepsy Behav. 2012;25(3):381-5. doi:10.1016/j.yebeh.2012.08.028.
21. Arhan E, Serdaroglu A, Aydin K, Hırfanoglu T, Soysal AS. Electroclinical features of epileptic encephalopathy with ESES: study of 59 patients. Seizure. 2015; 26: 86-93. doi:10.1016/j.seizure.2015.01.008.
22. Chen J, Yang Z, Liu X, Ji T, Fu N, Wu Y, et al. Efficacy of methylprednisolone for electrical status epilepticus during sleep in children. Zhonghua Er Ke Za Zhi. 2014;52(9):678-82.
23. Gencpinar P, Dundar NO, Tekgul H. Electrical status epilepticus in sleep/CSWS in children: EEG-based electroclinical evaluation. Epilepsy Behav. 2016; 61: 107-11. doi:10.1016/j.yebeh.2016.05.014.
24. Caraballo RH, Veggiotti P, Kaltenmeier MC, Piazza E, Gamboni B, Lopez Avaria MF, et al. Long-term multicenter study of encephalopathy with ESES/CSWS in 117 patients. Epilepsy Res. 2013;105(1-2):164-73. doi:10.1016/j.eplepsyres.2013.02.010.
25. Scheltens-de Boer M. EEG guidelines for encephalopathy related to ESES/CSWS in children. Epilepsia. 2009; 50 Suppl 7:13-7. doi:10.1111/j.1528-1167.2009.02211.x.

Authors' contribution

NA: Proposed topic, basic study design, material & methods and manuscript writing.
FZ: Data collection, statistical analysis and interpretation of result etc.
MY: Literature review & referencing and quality insurer.
S: Literature review and citation.
Z ur R: Data collection & literature review
AT: Data collection & literature review

All the authors have approved the final manuscript draft and accept the responsibility of research integrity.