e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(8); 1700-1703

Original Research Article

# An Observational Study on Clinical Profile and Risk Factors of Seizure

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**Received: 02-07-2025 / Revised: 01-08-2025 / Accepted: 02-09-2025**
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**Conflict of interest: Nil**

**Abstract:**

**Introduction:** Breakthrough seizures (BTS) occur despite antiepileptic therapy, often due to poor compliance or triggers like fever or sleep loss. Affecting 30–40% of treated children, BTS impact quality of life. This study assesses the incidence, clinical profile, and risk factors of BTS in Indian children aged 1–18 years.

**Methods:** This prospective observational study was conducted at Masonic Medical Centre for Children, Coimbatore (2018–2020), including 80 children aged 1–18 years with breakthrough seizures on AED therapy. Data on demographics, risk factors, clinical features, and investigations were collected. Ethical approval and informed consent were obtained before enrolment.

**Results:** Among 80 children with BTS, generalized seizures predominated. Significant associations were found between seizure frequency and age group, polytherapy, non-compliance, and fever. EEG findings and factors like video games, sleep deprivation, exertion, or stress showed no significant correlation. Fever emerged as the only notable trigger for increased seizure recurrence.

**Conclusion:** BTS frequency in children was significantly influenced by age, polytherapy, non-compliance, and fever. Generalized seizures predominated, while EEG findings and lifestyle factors showed no strong associations. Improved compliance, cautious use of multiple drugs, and prompt fever management are vital strategies to minimize BTS and enhance pediatric epilepsy outcomes.

**Keywords:** Breakthrough Seizures, Antiepileptic Drugs, Pediatric Epilepsy, risk factors, Seizures.



## Introduction

Breakthrough seizures (BTS) are defined as seizures that occur despite ongoing antiepileptic drug (AED) therapy, posing a significant clinical challenge in pediatric epilepsy management. These episodes may signal inadequate seizure control, medication non-compliance, or exposure to triggering factors such as fever, sleep deprivation, or intercurrent illness [1]. BTS affect approximately 30–40% of children on AED therapy, compromising quality of life and increasing the risk of injury and hospitalization [2]. The clinical profile and precipitating risk factors vary, with some studies indicating a higher occurrence among younger children and those with underlying neurodevelopmental disorders [3]. Identifying modifiable risk factors such as poor adherence, improper drug dosing, and avoidable triggers is essential for optimizing seizure control and reducing recurrence [4].

In the Indian context, limited data exist regarding the incidence and risk profile of BTS in children under active follow-up in pediatric neurology units. This observational study aims to estimate the incidence of BTS among children aged 1–18 years and to analyze their clinical characteristics and precipitating factors.

## Methods

It was a prospective, observational study conducted in the department of paediatrics, Masonic Medical Centre for Children, Coimbatore, Tamil Nadu. Study was conducted from October 2018 to 2020, 2 years. Ethical clearance was obtained from the Institutional Ethics Committee. Eligible patients and caregivers were briefed about the study, and written informed consent was obtained from those willing to participate.

Children aged between 1 and 18 years who presented with BTS despite being previously well-controlled on AED therapy for more than six months were included in the study. Children < 1 month,

those with anatomical abnormalities or neurological impairments such as cerebral palsy, hypoxic-ischemic encephalopathy (HIE), syndromic conditions, or stroke, as well as children with seizures secondary to metabolic causes or head injury, were excluded from the study.

The sample size was calculated using the formula $n = Z^2pq / E^2$, where Z is the reliability coefficient at a 95% confidence interval (1.96), p is the estimated proportion of the population with the characteristic of interest, q is 1–p, and E is the absolute precision, set at 5%. Since the exact prevalence of BTS in the study area was unknown, a conservative estimate of $p = 0.05$ was used. By substituting the values, with 10% marginal error the final sample size was confirmed to 80.

Data were collected on each patient's demographic profile including age, sex, and family history of seizures. Risk factors such as missed doses of antiepileptic medication, emotional stress, sleep deprivation, alcohol or recreational drug use, and screen exposure through TV or video games were recorded. Clinical details regarding the onset, symptoms, and signs during each breakthrough seizure episode were obtained from the patient, caregiver, and old medical records. All patients underwent a standardized diagnostic protocol that included a detailed history, physical examination, and relevant laboratory investigations such as complete haemogram, serum electrolytes, blood glucose levels, and neuroimaging when clinically indicated.

**Statistical analysis:** The collected data were entered into Microsoft Excel and analyzed using SAS software version 9.2 for Windows 10. Categorical variables such as sex, type of epilepsy, antiepileptic drugs, and precipitating factors were summarized using frequencies and percentages, while continuous variables like age, age at diagnosis, and seizure-free period were expressed as mean and standard deviation. Univariate analysis was performed to assess data distribution and identify associations between risk factors and seizures. Depending on data distribution, Chi-square or Fisher's exact test was applied, with Fisher's exact test found most suitable. A p-value $< 0.05$ was considered statistically significant.

**Results:**

Among 80 children with BTS, 73.75% had generalized, 21.25% focal, and 5% unclassified seizures. Focal cases showed a high rate (88.24%) of focal epileptic EEG findings, while 61.02% of generalized cases had no EEG performed. Statistical analysis showed a significant association between age group and BTS frequency ($P < 0.0001$), with toddlers (1–3 years) having more single seizures and preschool/school-aged children showing recurrence. A significant link was found between the number of antiepileptic drugs used and BTS frequency ($P < 0.0001$), with polytherapy associated with higher recurrence. Non-compliance was significantly associated with more frequent seizures ($P = 0.0297$). However, no significant associations were found with EEG findings ($P = 0.1812$), video games ($P = 0.8875$), sleep deprivation ($P = 0.4671$), exertion ($P = 0.2200$), or emotional stress ($P = 0.2875$). Fever was the only precipitating factor significantly linked to higher BTS frequency ($P = 0.0195$), suggesting it may be a critical trigger.

**Discussion**

In the present study involving 80 pediatric patients with BTS, the majority (73.75%) experienced generalized seizures, while 21.25% had focal seizures and 5% were unclassified. These findings are consistent with previous studies indicating that generalized seizures are more common in children compared to focal seizures due to the immature cortical networks and widespread neuronal excitability characteristic of the developing brain [5]. The high rate of generalized seizures also aligns with the natural course of many pediatric epilepsy syndromes, such as childhood absence epilepsy and generalized tonic-clonic seizures, which typically manifest during early developmental stages [6].

Electroencephalography (EEG) findings in our cohort revealed that 88.24% of children with focal seizures had corresponding focal epileptic discharges, whereas 61.02% of those with generalized seizures had not undergone EEG evaluation. Among those evaluated, a subset showed generalized epileptic findings or normal results. EEG plays a crucial role in characterizing seizure type, guiding AED selection, and monitoring disease progression [7]. However, the lack of EEG in over 60% of generalized seizure cases underscores diagnostic limitations, possibly due to resource constraints or acute settings, which may hinder timely neurological assessment [8]. The accuracy of EEG interpretation and its predictive value for seizure recurrence remain subjects of clinical debate, especially when abnormal findings are inconsistently distributed across seizure frequencies [9].

A statistically significant association between age group and frequency of BTS was observed ($P < 0.0001$), with toddlers (1–3 years) demonstrating a higher incidence of single seizures, while preschool (3–6 years) and school-aged children (6–12 years) experienced more recurrent episodes. This age-dependent variation in seizure recurrence may be attributable to several factors. Firstly, toddlers typically have a shorter duration of epilepsy diagnosis and may still be in early treatment phases, resulting in relatively better seizure control [10]. On the other hand, preschool and school-aged

children are more susceptible to triggering factors such as medication non-compliance, sleep disruption, and environmental stress, all of which can compromise seizure control and increase BTS frequency [1]. Additionally, longer duration of illness in older children may lead to pharmacoresistance or alterations in seizure threshold, further contributing to recurrence.

This age-related pattern is crucial for tailoring preventive strategies and counseling caregivers. Younger children with fewer recurrences may benefit from strict adherence to prescribed AED regimens and scheduled follow-up, while older children may require a more comprehensive approach, including behavioral interventions, school-based support, and regular therapeutic drug monitoring. Furthermore, these findings emphasize the need for early EEG assessment in all seizure types to ensure accurate classification and treatment planning. Future research should explore whether age-specific risk factors such as hormonal changes, cognitive load, or social environment contribute to seizure recurrence in pediatric populations.

In the present study, a statistically significant association was observed between the number of AEDs used and the frequency of BTS, with polytherapy linked to a higher rate of recurrence ($P < 0.0001$). Children receiving multiple AEDs tended to have more frequent seizures, which may reflect underlying pharmacoresistance or more severe forms of epilepsy. Polytherapy, although sometimes necessary in refractory cases, often increases the risk of adverse effects and drug interactions, which can compromise adherence and treatment effectiveness [11]. Previous studies have reported that monotherapy is sufficient in nearly 70–80% of pediatric epilepsy cases and is associated with better seizure control and fewer side effects [12]. The use of polytherapy should therefore be reserved for cases with confirmed resistance to single-agent treatment and should be accompanied by careful monitoring of drug levels and therapeutic response [13].

Non-compliance with prescribed antiepileptic regimens was also found to be significantly associated with increased BTS frequency ($P = 0.0297$). Children who skipped doses or failed to adhere to the treatment schedule were more likely to experience seizure recurrence. This observation is consistent with existing literature, which emphasizes that even brief interruptions in medication can lower the seizure threshold and precipitate episodes [1, 14]. Factors contributing to non-compliance include forgetfulness, lack of caregiver supervision, complex dosing schedules, and socioeconomic challenges [15]. Studies have shown that interventions such as caregiver education, reminder systems, and simplified drug regimens can significantly enhance adherence and reduce the risk of BTS [16]. These findings highlight the critical role of compliance in achieving and maintaining seizure control in pediatric patients.

Interestingly, the analysis did not show any statistically significant association between EEG findings and BTS frequency ($P = 0.1812$). While EEG remains a valuable tool for classifying seizure types and guiding initial therapy, its role in predicting seizure recurrence is limited. EEG abnormalities do not always correlate with clinical seizure activity, and normal EEGs can occur in epileptic patients during interictal periods [17]. Similarly, the study found no significant associations between BTS frequency and other commonly discussed precipitating factors such as video games ($P = 0.8875$), sleep deprivation ($P = 0.4671$), physical exertion ($P = 0.2200$), and emotional stress ($P = 0.2875$). Although these factors are frequently reported anecdotally or in smaller observational studies as potential triggers, larger studies and controlled analyses have failed to consistently demonstrate strong causal relationships. This suggests that while such factors may contribute to seizure vulnerability in some individuals, they are not universally predictive or statistically robust across broader pediatric populations.

Fever was the only precipitating factor found to be significantly associated with increased BTS frequency ($P = 0.0195$). Febrile illnesses can lower the seizure threshold, particularly in young children, by inducing inflammatory changes in the brain or altering drug metabolism and serum levels of AEDs [18]. Fever has long been recognized as a trigger for febrile seizures and may similarly act as a precipitating factor for BTS in children with underlying epilepsy [19]. Given the high prevalence of febrile illnesses in pediatric populations, especially in developing countries, this finding has practical clinical implications. Caregivers should be counseled to monitor for febrile episodes and manage them promptly using antipyretics and adequate hydration. In high-risk patients, temporary adjustment of AED dosage during illness may be considered under medical supervision to prevent BTS [20]. Overall, the study emphasizes the importance of individualized care, focusing on medication compliance, cautious use of polytherapy, and proactive management of febrile illnesses to minimize BTS in children with epilepsy.

## Conclusion

This study highlights that generalized seizures are the most common type of BTS in children, with a significant association between BTS frequency and factors such as age group, number of antiepileptic drugs, medication compliance, and fever. Polytherapy and non-compliance were linked to increased recurrence, emphasizing the need for simplified regimens and caregiver education. EEG

findings and other potential triggers like sleep deprivation, video games, or emotional stress were not significantly associated. Early intervention during febrile episodes may reduce seizure risk. Tailored treatment approaches and proactive management are essential to improve seizure control and quality of life in pediatric epilepsy.

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