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Original Research Article

# A Prospective Observational Investigation of the Etiological Profile and Prognosis of Children with Status Epilepticus Involved in a Tertiary Care Hospital

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**Abstract:**

**Objective:** The purpose of this research was to describe the clinical-etiological profile of Status Epilepticus (SE) in children under the age of 11 and to investigate the risk factors, etiologies, outcomes at the end of hospitalization, and predictors of favorable/unfavourable outcomes in SE.

**Method:** This was a hospital base prospective study of 100 children under the age of 11 who were admitted consecutively with SE to a pediatric intensive care unit of a tertiary care referral hospital in Patna Medical College & Hospital, Patna for a year, from April 2021 to April 2022, were enrolled in the study. The principal investigator gathered and entered the data regarding the parameters in a standardized proforma after a thorough review and necessary inquiries. The final result was documented after the patient's hospital stay. The acquired data were evaluated to find important variables that might predict the result and the risk factors for RSE.

**Results:** After infancy, the age range of 2 to 5 years was reported to have the highest prevalence of SE. 48.7% of cases involved girls, while 51.3% involved boys. Meningoencephalitis and febrile status were the two most frequent causes of status. Anemia was found to be a risk factor (odds ratio=8.67) and to be substantially linked with RSE (p value=0.002). 8 (8%) of the kids died. Moreover, a worse result was seen more frequently in children who remained pain sensitive or unresponsive 5 hours following seizure control (p-value <0.02). The advancement of RSE and worse results were substantially linked to delaying the administration of the first anti-epileptic drug (AED).

**Conclusion:** Anemia and a delay in starting the first AED were discovered to be strongly linked with RSE. Also, there was a strong correlation between poor outcomes and kids who were still in pain or unresponsive 6 hours following seizure control.

**Keywords**: mortality, meningitis, febrile state, anemia, and antiepileptic drugs.



## Introduction

Although there have been improvements in therapy, status epilepticus (SE) is still the most frequent neurological emergency in children and is linked to high morbidity and death [1,2; Figure 1]. Most status cases that are referred to a tertiary care facility are on the severe end of the range. Hence, information from admissions to the Pediatric Intensive Care Unit (PICU) for SE may offer some insight into the factors that influence how severe SE is and make it easier to devise effective ways to lessen the severity.

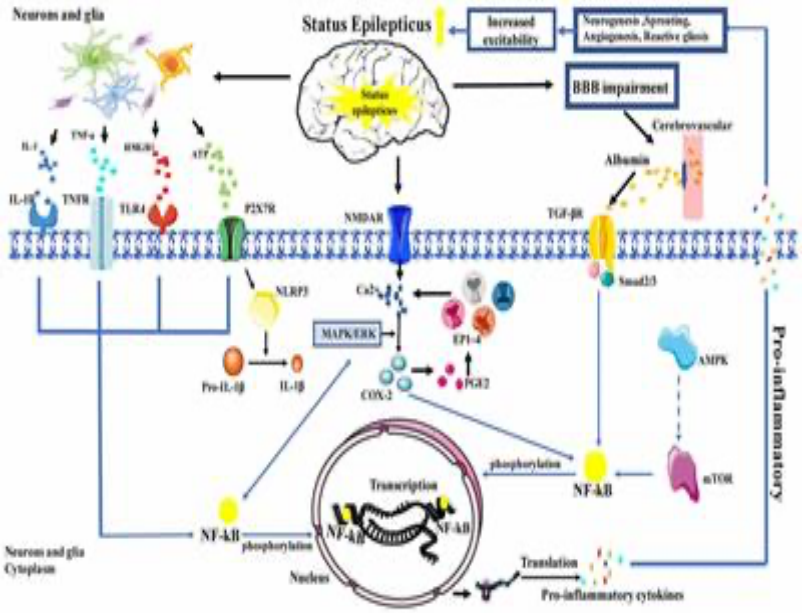


**Figure 1: A Network in Status Epilepticus Pathogenesis**

Despite this, investigations on pediatric SE admissions to PICU are uncommon. In children, the risk factors for refractory status epilepticus (RSE) are less well understood.

Also, the majority of information on RSE comes from industrialized nations and epidemiological studies that included data on adults and children [3,4] or contained information on both types of SE (abortive and refractory).

**Method:**

For one year, from April 2021 to April 2022, a prospective observational study of all consecutive children up to the age of 11 who were admitted with status epilepticus to the PICU of a tertiary care referral facility in Patna Medical College & Hospital, Patna was conducted. Infants (less than one month old) were not included.

Less than 2 years, 1–5 years, and 6–11 years were used to categorise the age group. This was done in order to compare the age range in which febrile seizures are most prevalent and to take into account the literature's claim that babies had a greater prevalence of status (1-5 years).

Data were examined and entered after rigorous inspection and the necessary blood tests. An investigation of the cerebrospinal fluid (CSF) was performed on a febrile youngster after stabilising him or her and ruling out increased intracranial pressure.

Infants under the age of five months had their CSF examined as well because meningitis symptoms may not be obvious at this age and a fever may not even be present. Depending on the condition of the child, computed tomography (CT) or magnetic resonance imaging (MRI) were performed in each case. All RSE patients underwent electroencephalography (EEG). AVPU scale was used to evaluate the sensory system (A-alert, V-verbal, P-pain responsive, Unresponsive).

Standard treatment recommendations were used to address seizures [5]. Any difficulties that developed following the administration of AEDs were regarded as drug-related issues. At the conclusion of the hospital stay, the final diagnosis and outcome were reported.

Clearance from the institution's ethical committee was obtained. The carers provided written informed permission in both the local language and English. There were no additional costs for the patient.

**Results:**

During the study period, 111 kids who met the inclusion criteria were enrolled (n = 100). 51.3% of the subjects, or 55, were boys. 8 months was the youngest age analysed, while 11 years was the oldest. The majority (52) of the children were between the ages of 1 and 5 (47.6%), with 48 (39.5%) being infants.

The mean age was 2.8 years, with a standard deviation of 3.02, and 69 (72.0%) of the patients had generalised tonic-clonic seizures (GTCS), 20 (18.9%) had focal seizures, and 11 (8%), which began as focal seizures but eventually turned into GTCS. Of the 40 (36.8%) people with a history of seizures, 18 (48.7%) were febrile and 22 (51.3%) were not.

Among the 100 individuals, 60 (54.8%) had a history of seizures; the majority, 45 (76%) had a history of febrile seizures. 80 kids (or 71%) were referred by several main and secondary care hospitals, both public and private.

Among the children who were referred, 74 (93.7%) received their first dosage of AED from the referring institution. Eighty cases of status were resistant (72.8% of all cases), and four were extremely resistant (4.4% of all cases). Boys were more likely to have refractory status in the age range up to 5 years, however this link was not statistically significant (p-value=0.303).The results of the investigations are listed in Table 1. It was discovered that there is no connection between refractory status and a history of birth asphyxia, developmental delay, prior seizure history or family history, elevated C - reactive protein (CRP), or abnormal brain imaging.

**Table 1: Status epilepticus laboratory profile in children**

| Parameter | No. of cases | Percentage of cases |
|---|---|---|
| Anemia | 32 | 29.6% |
| Leukocytosis | 41 | 39.5% |
| Leukopenia | 6 | 6.2% |
| Thrombocytopenia | 6 | 6.2% |
| CRP | 36 | 33.2% |
| Hypoglycemia | 5 | 5.3% |
| Hyperglycemia | 1 | 1.7% |
| Hypocalcemia | 1 | 1.7% |
| Hyponatremia | 11 | 10.57% |
| Hypomagnesemia | 1 | 1.7% |
| Acute Kidney Injury | 5 | 5.3% |
| Abnormal Liver Function test | 7 | 7.7% |
| INR | 7 | 7.7% |
| Abnormal brain imaging | 31 | 29.6% |
| Abnormal EGG | 41 | 37.7% |

Based on the AVPU scale, the sensorium was evaluated. A significant association between anaemia and refractory status was found (p value = 0.002), and anaemia was found to be a risk factor for status becoming refractory (odds ratio=8.67). Five hours after seizure control, the majority of children—52 (47.6%) became verbal, 16 (15.2%) became alert, 38 (35.0%) remained pain responsive, and 1 (1.7%) remained unresponsive. Compared to febrile state, elevated CRP was strongly related with meningitis (p value = 0.07). (Table 2).

**Table 2: Distribution of elevated CRP (C - reactive protein) with meningoencephalitis and a feverish state**

| CRP | Febrile State | Meningitis | Stastical Analysis |
|---|---|---|---|
| Raised CRP | 7 (15%) | 16 (70.7%) | Chi Square=21.794 |
| Normal CRP | 43 (85%) | 6 (29.1%) | P-Value < 0.02<br>Odds Ratio=0.77<br>95% CI=0.024 TO 0.24 |

95 (94.4%) children with status had EEGs. All kids with RSE were included in this. In other circumstances, EEG could only be performed when status was under control. Refractory status was seen in 34 (83.2%) of the kids with abnormal EEGs, and the p value was 0.04.

While most children with infections of the Central Nervous System (CNS) showed normal brain imaging, cortical hyperintensities were found in 11 children with meningoencephalitis, including 1 with Herpes Simplex Virus (HSV) encephalitis. Regarding the final diagnosis, meningoencephalitis was the most common, with 23 cases (21.5%) followed by 50 cases (45.8%) of fever. Meningoencephalitis-21 (24.5% of RSE) and febrile status 34 (43.1% of RSE) were shown to be the two most frequent causes of RSE.

One child had HSV encephalitis, seven had meningitis that had been confirmed by CSF culture, and other kids had suspected encephalitis. The least frequent causes were cerebral bleeding and autoimmune encephalitis. Throughout their stay in the PICU, 24 (22.4%) children needed mechanical ventilation. At discharge, the kids were divided into those who had positive results (returned to baseline or normal) and those who had negative results (new FND or death). The results showed that although 25 (21.5%) had an unfavourable outcome, 85 (78.3%) did. There were 8 fatalities (8.0%). Children with unfavourable outcomes were more frequently those who remained pain responsive or unresponsive 5 hours following seizure control. P value < 0.02 indicated that this connection was significant. Moreover, children who had a poor outcome (20 out of 23, or 87.4%) were more likely to have refractory status than those who had a good outcome (61 out of 86, or 68.8%) (p value = 0.06). Before referral, diazepam was the most frequently administered first AED. Only 2 (2.6%) participants

used midazolam as their first AED, while 47 (48.5%) subjects used diazepam and 51 (45.7%) used lorazepam. The first AED most frequently administered by the research centre was lorazepam. Fosphenytoin was the second AED administered by the research centre, and levetiracetam came next. Maximum 53 of the 80 resistant youngsters (66.5%) were under levetiracetam's control. Phenobarbitone, Valproate, Thiopentone, Midazolam infusion, and Lacosamide were other AEDs used in the PICU. Eight AEDs were employed, at most, to control seizures in two children with idiopathic causes.

15 of the 90 children (17.4%) who received the first AED quickly (within 20 minutes of their seizures) had a poor result at discharge, making up 62 of the 90 (69.2%) children who had refractory seizures. In comparison, 7 of 21 patients (41%) had a poor result at discharge and 17 of 21 (91%) experienced refractory seizures after receiving the first AED after 20 minutes (p value = 0.04). Refractoriness was not observed to be significantly impacted by the time between the first and second AED (p value = 0.06).

**Discussion:**

Of the 100 children with status epilepticus we evaluated, majority (51.3%) swere boys. The age range of 1 to 5 years was shown to be the most impacted (47.6%), followed by infancy (39.5). The prevalence of convulsive status epilepticus is higher in younger age groups, according to a number of studies. This could be because acute symptomatic reasons are more common in this age group and because the developing brain is more prone to seizures [6].

More than 91% of the individuals came from lower socioeconomic backgrounds, which may be related to the fact that the study centre offers free childcare to kids as part of a number of government-approved programmes. Children were referred to other outside hospitals in 71% of cases Children were referred to other outside hospitals in 71% of cases. Other children (93.7%) had been referred after the first AED was administered, with the exception of 4 (6.2%) of the referred kids.

The majority of kids in our study (72.8%) advanced to RSE. This might occur as a result of the study's lack of consideration for seizure duration when defining RSE. The similar definition of refractory status was utilised in a two-year multi-center study conducted in the United Kingdom (Tully et al) [7]. Less children were categorised as having RSE in trials where the extra requirement of lasting longer than 60 minutes was included in the criterion [8].

Meningoencephalitis (21%) and febrile status (45.8%) were the two most frequent causes of status in this investigation. Meningoencephalitis and febrile status were found to be the most frequent causes of RSE, respectively. According to studies and other literature, fever is the most frequent cause of status epilepticus in children, especially those under the age of six. Whereas older children are more likely to have remote or cryptogenic origins, younger children are more likely to have a feverish condition and an acute symptomatic aetiology [7]. Due to the lack of clear Brain involvement in febrile seizures, children with febrile status were examined separately in some studies while being included in the acute symptomatic group in others [9].

Evidence from the literature supports the findings of our study that children with refractory status had worse outcomes and higher mortality than those with abortive status [10,11]. We also discovered that children who remained pain responsive or unresponsive 5 hours following seizure control had a worse prognosis more frequently. The significance of this connection was 0.02 (p value). This should be used as a criterion for status epilepticus outcome prediction in additional investigations.

Although the majority of our children had received their first AED from the referral center, we discovered that delays in receiving the first AED had a substantial impact on refractory seizures and unfavourable discharge outcomes. Most often, this delay was caused by the time it took for patients to travel from their homes to the closest medical facility and then to our hospital. Several pieces of evidence indicate that timely AED delivery from the referring centre and minimising delays in treatment commencement greatly enhanced result [12,13]. Evaluation, care, and transportation of the critically ill kid to the proper facility are significantly impacted by inadequately organised pre-hospital services [14].

We discovered a strong correlation between anaemia (93.8%) and refractory status. Anemia was discovered to be a risk factor for refractory status (odds ratio: 8.67). Meningitis was substantially more likely to be linked to elevated CRP (70.6%) than being febrile (14%) ($p< 0.02$). These parameters in blood examinations have not been examined by other RSE studies, and additional research is needed to validate the same.

There were 8 deaths (8.0%). Mortality rates between 12 to 32% have been recorded in previous investigations [15]. Studies have found lower mortality rates, primarily in populations from the west [16]. This disparity in mortality may be caused by the fact that in poor nations, children who are referred to tertiary centres have very severe/prolonged seizures for which the primary and secondary centres' initial therapeutic efforts have proven ineffective. Moreover, children in

developing nations are more likely to experience acute symptomatic reasons including CNS infections, which are linked to greater mortality. Also, because of the longer wait before starting treatment, these kids experience additional difficulties [17]. There aren't many research on the effectiveness of EEG in paediatric SE. 90% of children who present with seizures had EEG abnormalities, however these were performed hours to days later [18].

While choosing chronic AED therapy for the patient, it is crucial to know if the seizure is focal or generalised. One-third of children who receive EEG monitoring are reported to develop electrographic seizures after convulsive seizures, and among these, one-third only have electrographic seizures [19].

**Conclusion:**

Refractory status is not significantly associated with a history of birth asphyxia, developmental delay, previous seizure history, family history of seizures, elevated CRP, or abnormal brain imaging. Meningoencephalitis and febrile state were the two most frequent causes of SE and RSE. The progression to refractory status and subsequent adverse outcomes were substantially linked with delaying the administration of the initial anti-epileptic medication.

This was mostly caused by how long it took the patient to get to the closest medical facility, which highlights the need to increase prehospital care and first aid procedures. Anemia was discovered to be a risk factor (odds ratio=8.67) and was substantially connected with refractory status (p value=0.002). Unfavorable outcomes were more frequently linked to kids who were still awake or unresponsive 5 hours following seizure management. The p-value for this connection was significant ($P < 0.02$).

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