

# Study of etiological profile and neurological outcome of children's presenting with status epilepticus

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## Abstract

**Background:** Status epilepticus is a neurological emergency requiring immediate evaluation and management to prevent significant morbidity or mortality. The short-term mortality (within 30 days) of SE ranges from 7.6% to 22% across all age groups and is highest amongst the elderly. Present study was undertaken to provide additional information about etiological profile and neurological outcome of children's presenting with status epilepticus. **Material and Methods:** Present study was prospective and observational study, conducted in children of age 1 month to 12 years who presented with status epilepticus. **Results:** Maximum numbers of male and female patients were in the age group of 2 to 5 years (46%) followed by 5 to 10 years (28%). In present study, in majority of cases age of 1st onset of seizure was 6-12 months (23%), GTCS was the commonest type of seizure (97%), focal Neurological deficit was seen in 24% cases, Prehospital resuscitation was done in 31% cases. Most common symptom was vomiting (35%) followed by fever with URI (22%) and ALOC (20%) Most common etiology associated with status epilepticus in children was seizure disorder 44% (44 cases), next being acute CNS infection 34% (34 cases), fever provoked seizures 24% (24 cases) and Quadriplegia 19% (19 cases). Out of 20 children with abnormal neuroimaging, 7 children had refractory status epilepticus (RSE). 76 cases (76%) recovered. Among those recovered, 6 cases (6%) recovered with new neurological sequel; 13 cases (13%) died and 5 cases (5%) discharged against medical advice (AMA). **Conclusion:** Male preponderance and younger age at presentation were the highlights. The commonest type of seizure was a generalised tonic-clonic seizure. Seizure disorder, acute CNS infections, and febrile seizures were commonest etiological.

**Keywords:** Status epilepticus, Seizures, generalised tonic-clonic seizure, Neuroimaging

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## INTRODUCTION

Status epilepticus is a neurological emergency requiring immediate evaluation and management to prevent

significant morbidity or mortality. According to International League Against Epilepsy (ILAE) defines status epilepticus as a seizure which shows no clinical sings of an arresting after a duration encompassing the great majority of seizures of that type in most patients or recurrent seizures without resumption of baseline central nervous system function interictally.<sup>1</sup> An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.<sup>1</sup> A seizure that lasts longer than 5 minutes, or having more than 1 seizure within a 5 minutes period, without returning to a normal level of consciousness between episodes is called status epilepticus. This is a medical emergency that may lead to permanent brain damage or

death.<sup>2</sup> The reported mortality at hospital discharge in SE is 9–21%. The short-term mortality (all age groups) rates reported from India and other developing countries range between 10.5% and 28%.<sup>3</sup> The short-term mortality (within 30 days) of SE ranges from 7.6% to 22% across all age groups and is highest amongst the elderly.<sup>4</sup> Present study was undertaken to provide additional information about etiological profile and neurological outcome of children’s presenting with status epilepticus.

### MATERIAL AND METHODS

Present study was prospective and observational study, conducted in Department of Pediatrics, Swami Ramanand Teerth Rural Government Medical College, Ambajogai, India. Study duration was of 2 years (1st November 2018 to 31st October 2020). The study was commenced after the institution ethical committee clearance.

**Inclusion criteria:** Children of age 1month to 12 years who presented with status epilepticus

**Exclusion criteria:** Child with status epilepticus with head injury. Children less than 1 month and more than 12 years of age. Patients whose parents do not give consent.

All consecutive cases of status epilepticus-those admitted during the study period. All children who met the inclusion criteria were enrolled in the study and informed consent was obtained from their parents/guardian. A detailed history in all cases was taken with emphasis on the onset

of seizure, duration of seizure, number of convulsion, type of seizure, antenatal, natal and postnatal risk factors. Thorough clinical examination was done – vitals, general physical examination and systemic examination with special reference to central nervous system. All relevant investigations to arrive at the diagnosis and further management performed; children were followed up to evaluate their immediate outcome. i.e., till discharge or death.

Data entered in Microsoft-Excel sheet and its analysis performed by the statistical software SPSS. Chi square test and Fischer test are used for nominal data. ‘P’ value less than 0.05 was considered statistically significant.

### RESULTS

A total 100 Children’s of age 1month to 12 years who presented with status epilepticus were enrolled in the study. A total 100 Children’s of age 1month to 12 years who presented with status epilepticus were studied during this study period. Maximum numbers of male and female patients were in the age group of 2 to 5 years (46%) followed by 5 to10 years (28%) then less than 2 years (20%) and 10-12 years (6%). The mean age of patients was 3.75 ± 2.43 years. There was no statistically significant difference in male and female according to age distribution (p>0.05)

**Table 1:** Distribution of the Study subjects according to Age and gender

| Age group (in years) | Males     | Females   | Total      | Percentage  |
|----------------------|-----------|-----------|------------|-------------|
| <2                   | 13        | 07        | 20         | 20%         |
| 2 to 5               | 26        | 20        | 46         | 46%         |
| 5 to10               | 15        | 13        | 28         | 28%         |
| 10 to12              | 04        | 02        | 06         | 6%          |
| <b>Total</b>         | <b>58</b> | <b>42</b> | <b>100</b> | <b>100%</b> |

Maximum numbers of children were born after 37 weeks gestation (term pregnancy) while 5% children born before 37 weeks (pre-term), more commonly known as premature. Most of the children 55% were born as 1<sup>st</sup> child followed by 2<sup>nd</sup> order of birth were 35%. Institutional birth was most common in 99% cases. NICU candidate were 60% and most common factor for addition in NICU was respiratory distress syndrome (RDS) 16% followed by neonatal sepsis (NNS) 13% and early onset sepsis (EOS) 11%. Duration of breastfeeding <6 months was in 44% cases and 6-12months in 45%.

**Table 2:** Distribution of study subjects according to Birth characteristics

| Birth characteristics |                               | No. of Cases | Percentage |
|-----------------------|-------------------------------|--------------|------------|
| Term                  | SGA                           | 05           | 95%        |
|                       | AGA                           | 90           |            |
| Preterm               | SGA                           | 02           | 5%         |
|                       | AGA                           | 03           |            |
| Order of birth        | 1                             | 55           | 55%        |
|                       | 2                             | 35           | 35%        |
|                       | 3                             | 08           | 8%         |
|                       | >3                            | 02           | 2%         |
| Place of birth        | Home                          | 01           | 1%         |
|                       | Institution                   | 99           | 99%        |
| NICU Candidate        | neonatal hyperbilirubinemia   | 13           | 13%        |
|                       | respiratory distress syndrome | 16           | 16%        |
|                       | early onset sepsis            | 11           | 11%        |

|                           |   |    |     |
|---------------------------|---|----|-----|
|                           | neonatal sepsis                         | 09 | 9%  |
|                           | low birth weight /Very low birth weight | 06 | 6%  |
|                           | meconium aspiration syndrome            | 05 | 5%  |
| Duration of breastfeeding | <6 months                               | 44 | 44% |
|                           | 6-12 months                             | 45 | 45% |
|                           | 1-2 years                               | 10 | 10% |
|                           | >2 years                                | 01 | 1%  |

History of iron deficiency anaemia was observed in 5% cases, Stroke in 11%, space occupying lesion in 6%, CNS Malformation 6%, Immunization appropriate in 96%, milestones appropriate for age in 73% and delay in 27%. History of failure to thrive observed in 24% and vitamin/micronutrient deficiency was observed in 20%.

**Table 3:** Distribution of study subjects according to Past history

| Past history  | No. of Cases | Percentage |
|---|--------------|------------|
| H/O Iron deficiency anaemia   | 5            | 5%         |
| H/O Stroke  | 11           | 11%        |
| space occupying lesion  | 6            | 6%         |
| CNS Malformation  | 6            | 6%         |
| Not appropriate Immunization as per national immunization programme | 04           | 4%         |
| Delayed milestones  | 27           | 27%        |
| H/O failure to thrive   | 24           | 24%        |
| Vitamin/Micronutrient deficiency                                    | 20           | 20%        |

In present study, in majority of cases age of 1st onset of seizure was 6-12 months (23%) followed by 2-6 months (22%) and 5-10 years (21%). GTCS was the commonest type of seizure seen in 97 cases (97%) and focal seizure with secondary GTCS observed in 3(3%) cases. In most of the cases (24%) 2-4 times recurrence of seizure was observed since 1st diagnosis followed by 10-20 times in 15%, 5-10 times in 14, <2 times in 9 and >20 times in only one child. Focal Neurological deficit was seen in 24% cases, Positive family history in 11%, preceding aura 46%. The maximum number of children presented with fever of 100-104 F (53%) and 8% child with 105-106 F. Duration of fever was <2 days in 40% cases, between 4-8 days in 14%, 2-4 days in 13% and in one child duration of fever was >8days.

**Table 4:** Spectrum of clinical presentation

| Clinical presentation                | No. of Cases | Percentage |
|--------------------------------------|--------------|------------|
| Age of 1st Onset                     |              |            |
| < 2 month                            | 11           | 11%        |
| 2-6 months                           | 22           | 22%        |
| 6-12 months                          | 23           | 23%        |
| 1-5 years                            | 19           | 19%        |
| 5-10 years                           | 21           | 21%        |
| >10 years                            | 04           | 4%         |
| Seizure presentation                 |              |            |
| general tonic clonic seizures (GTCS) | 97           | 97%        |
| Focal seizures                       | 00           | 0.0%       |
| Focal with secondary GTCS            | 03           | 3%         |
| Myoclonus                            | 00           | 0.0%       |
| Recurrence since 1st diagnosis       |              |            |
| <2 times                             | 09           | 9%         |
| 2-4 times                            | 24           | 24%        |
| 5-10 times                           | 14           | 14%        |
| 10-20 times                          | 15           | 15%        |
| >20 times                            | 01           | 1%         |
| Focal Neurological deficit           | 24           | 24%        |
| Positive family history              | 11           | 11%        |
| Preceding aura                       | 46           | 46%        |
| Temperature                          |              |            |
| <100F                                | 08           | 8%         |
| 100-104 F                            | 53           | 53%        |
| 105-106 F                            | 08           | 8%         |
| Fever duration                       |              |            |

|          |    |     |
|----------|----|-----|
| < 2 days | 40 | 40% |
| 2-4 days | 13 | 13% |
| 4-8 days | 14 | 14% |
| >8 days  | 01 | 1%  |

Prehospital resuscitation was done in 31% cases. Most common symptom was vomiting (35%) followed by fever with URI (22%) and ALOC (20%) while the commonest sign was pallor (70%) followed by abnormal skull shape in 19% and syndromic appearance (10%). Majority of patients had- CBG in the ranged from 120 to 200 mg/dl (50%) followed by from 54 to 120 mg/dl. Sodium, potassium and calcium were low in 18%, 21% and 33% of cases respectively. Ongoing NCSE was present in 66% patients and intracranial pressure in 36%, clinical meningeal signs in 31%, involuntary movements was seen in 38%, Cerebellar signs in 6%. Urinary incontinence (Incontinence bowel/bladder) occurs in 38% child with status epilepticus.

**Table 5: Clinical examination profile of study population**

| Clinical Examination                     | No. of Cases | Percentage |
|--|--------------|------------|
| Prehospital resuscitation                | 31           | 31%        |
| Predominant post ictal presentation      |              |            |
| Vomiting                                 | 35           | 35%        |
| Fever                                    | 8            | 8%         |
| Acute watery diarrhoea                   | 18           | 18%        |
| Abdominal pain                           | 10           | 10%        |
| Lethargy                                 | 13           | 13%        |
| Crying during micturition                | 05           | 5%         |
| Fever + Upper respiratory infection      | 22           | 22%        |
| Fever + Urinary tract infection          | 01           | 1%         |
| Fever + Acute gastro enteritis           | 03           | 3%         |
| Altered Level of Consciousness           | 20           | 20%        |
| Oliguria                                 | 01           | 1%         |
| Clinical signs                           |              |            |
| Pallor                                   | 70           | 70%        |
| Icterus                                  | 03           | 3%         |
| Clubbing                                 | 01           | 15%        |
| Lymphadenopathy                          | 00           | 0.0%       |
| Oedema                                   | 01           | 1%         |
| Abnormal skull shape                     | 19           | 19%        |
| Syndromic appearance                     | 10           | 10%        |
| Cutaneous markers                        | 01           | 1%         |
| Others                                   | 06           | 6%         |
| capillary blood glucose (CBG) mg/dl      |              |            |
| <54                                      | 01           | 1%         |
| 54-120                                   | 40           | 40%        |
| 120-200                                  | 50           | 50%        |
| >200                                     | 09           | 9%         |
| Dyselectrolytemia                        |              |            |
| Na+ Low                                  | 18           | 18%        |
| K+ High                                  | 03           | 3%         |
| K+ Low                                   | 21           | 21%        |
| Ca+ Low                                  | 33           | 33%        |
| Ongoing Nonconvulsive status epilepticus | 66           | 66%        |
| intracranial pressure clinical features  | 36           | 36%        |
| Clinical meningeal signs                 | 31           | 31%        |
| Involuntary movements                    | 38           | 38%        |
| Cerebellar signs                         | 06           | 6%         |
| Incontinence bowel/bladder +             | 38           | 38%        |

Most common etiology associated with status epilepticus in children was seizure disorder 44% (44 cases), next being acute CNS infection 34% (34 cases), fever provoked seizures 24% (24 cases) and Quadriplegia 19% (19 cases).

**Table 6: Etiology and diagnosis profile**

| Diagnosis                | No. of Cases | Percentage |
|--------------------------|--------------|------------|
| Seizure disorder         | 44           | 44%        |
| Fever provoked seizures  | 24           | 24%        |
| Unprovoked seizures      | 09           | 9%         |
| Toxic encephalopathy     | 03           | 3%         |
| Autoimmune encephalitis  | 04           | 4%         |
| Acute CNS infection      | 34           | 34%        |
| Stroke                   | 08           | 8%         |
| Quadriplegia             | 19           | 19%        |
| Other - Systemic illness | 03           | 3%         |

SEPSIS Screen was positive in 93% cases, TORCH Screen positive in 8%, Viral Serology positive in 13% and Blood culture positive in 11%. CSF analysis was done for 81 children, cytology positive in 25%, Biochemistry positive in 30%, Culture/Sensitivity positive in 25% and CBNAAT positive for TB in 1 child. USG imaging study was done for 32 cases and USG abnormal in 26% cases, CT brain was done for 84 cases and 48 cases had abnormal findings. MRI done for 52 cases, 43% showed abnormal findings. Majority of children had abnormal epileptiform activity (73%). Out of 20 children with abnormal neuroimaging, 7 children had refractory status epilepticus (RSE). Among the structural abnormality, most common was cystic encephalomalacia seen in 30% cases followed by porencephaly 20%, space occupying lesion-DNET 20%, polymicrogyria cortex 20 and arachnoid cyst in temporal region seen in 10% cases.

**Table 7: Investigation profile of study population**

| Parameters                          | No. of patients | Percentage |
|-------------------------------------|-----------------|------------|
| SEPSIS Screen positive              | 93              | 93%        |
| TORCH Screen positive               | 08              | 8%         |
| Viral Serology positive             | 13              | 13%        |
| Blood culture positive              | 11              | 11%        |
| CSF analysis                        |                 |            |
| Cytology positive                   | 25              | 25%        |
| Biochemistry positive               | 30              | 30%        |
| Culture/Sensitivity positive        | 25              | 25%        |
| CBNAAT positive for TB              | 01              | 1%         |
| Imaging study                       |                 |            |
| USG positive                        | 26              | 26%        |
| CT brain positive                   | 48              | 48%        |
| MRI brain positive                  | 43              | 43%        |
| EEG- Abnormal epileptiform activity | 73              | 73%        |
| Structural abnormality              |                 |            |
| Cystic encephalomalacia             | 06              | 30%        |
| Porencephaly                        | 04              | 20%        |
| Space occupying lesion-DNET         | 04              | 20%        |
| Polymicrogyria cortex               | 04              | 20%        |
| Arachnoid cyst in temporal region   | 02              | 10%        |

Mean duration of hospital stay was 7 days and 16 . 10 children (10%) were discharged within 5 days after admission. 59 children (59%) were discharged within 15 days and 29 (29%) children were discharged within 25 days after admission. Prolonged hospital stay of >25 days observed in 2 cases.

**Table 8: Number of days of hospital stay**

| Hospital stay (days) | No. of patients | Percentage |
|----------------------|-----------------|------------|
| <5                   | 10              | 10%        |
| 5-10                 | 31              | 31%        |
| 10-15                | 28              | 28%        |
| 15-20                | 17              | 17%        |
| 20-25                | 12              | 12%        |
| >25                  | 02              | 2%         |

Out of 100 cases, 76 cases (76%) recovered. Among those recovered, 6 cases (6%) recovered with new neurological sequel; 13 cases (13%) died and 5 cases (5%) discharged against medical advice (AMA).

**Table 9: Final outcome**

| Outcome                  | No. of Patients | Percentage  |
|--------------------------|-----------------|-------------|
| Recovered without sequel | 76              | 76%         |
| Recovered with sequel    | 06              | 6%          |
| Death                    | 13              | 13%         |
| AMA                      | 05              | 5%          |
| <b>Total</b>             | <b>100</b>      | <b>100%</b> |

## DISCUSSION

Status epilepticus is a common paediatric neurological emergency with an estimated incidence of 18–23 per 100,000 children per year and a mortality of 2%–7%.<sup>5</sup> In developing countries, optimal management of status epilepticus is associated with major barriers such as poor health care infrastructure, delay in transportation, lack of ambulance services, intermittent availability of drugs and economic affordability.<sup>6</sup> In present study male predominance was noted, which was not statistically significant. Similar findings were noted by Thandavarayan *et al.*,<sup>7</sup> study out of 92 children, male children were 46 (50%) and female children were 46 (50%). Likewise, in Vafaee-Shahi *et al.*,<sup>8</sup> study the prevalence of S.E in male and female children was 57.1% and 42.9%, respectively. Male to female ratio in our study was found to be 1.38:1. Predominant involvement of younger age group has been reported previously in many studies.<sup>3,5,9</sup> The reason for this predominance is probably, mechanisms for control of seizure activity are fragile in younger children and may get disrupted with minimal abnormalities in neurofunction. Also, younger age is more vulnerable for acute etiologies including febrile seizures. 54% of our cases presented as SE without prior history of seizures. Purusothaman and Kumar<sup>10</sup> reported 40.7% children presented as SE without a prior history of seizures. 53.3% by Gulati *et al.*<sup>11</sup>, in Kumar *et al.*<sup>3</sup> study 74.2% cases presented with SE without any prior history of seizures and 18 patients (25.7%) had one or more seizure episodes in the past. Therefore, it was observed that association of prior seizure episodes with occurrence of SE was not significant ( $p > 0.005$ ). GTCS was the commonest type of seizure seen in 97 cases (97%) and focal seizure with secondary GTCS observed in 3(3%) cases which is comparable with study done by Purusothaman and Kumar<sup>10</sup> where a generalized tonic-clonic seizure was the most common type 77.7% and Focal seizures observed in 2(3.7%). The most common seizure type observed in the Gulati *et al.*<sup>11</sup> study was GTCS (63.3%), which is similar to the present study. The aetiological spectrum of SE in developing countries is distinctly different when compared to developed countries. In present study, the most common etiology associated with status epilepticus in children was seizure disorder (44%), next being acute CNS infection (34%), fever provoked seizures (24%) and Quadriplegia (19%). In developing countries CNS infections accounted for 28–67% of

aetiological spectrum<sup>6,12</sup> and this was much more so in the paediatric age group<sup>12,13</sup>. In the studies from developed countries, the reported frequency of CNS infections as the risk factor varied from 4% to 19%<sup>14</sup>. In Thandavarayan *et al.*,<sup>7</sup> study the most common etiology associated with SE in 92 children was remote causes 27.2%, next being acute CNS infection (19.6%), febrile seizure (18.5%) and cryptogenic/idiopathic SD (16.3%). Murthy *et al.*,<sup>14</sup> reported CNS infection accounts for significant number of cases. The etiology of seizures is usually analysed because this has been shown to affect the morality of SE and can affect the duration of seizures.<sup>15</sup> Neuroimaging of children with status epilepticus showed that out of 20 children with abnormal neuroimaging, 7 children had refractory status epilepticus (RSE). In Purusothaman and Kumar<sup>10</sup> study, structural abnormality was seen in 10 (18.5%) cases of them 7 children (12.2%) presented with refractory status epilepticus. Out of 100 cases, 76 cases (76%) recovered. Among those recovered, 6 cases (6%) recovered with new neurological sequelae; 13 cases (13%) died and 5 cases (5%) discharged against medical advice (AMA). In Thandavarayan *et al.*,<sup>7</sup> study out of 92 cases, 74 cases (75%) recovered. Among those recovered, 5 cases (5.5%) recovered with new neurological sequelae; 13 cases (14%) died and 5 cases (5.5%) discharged against medical advice (AMA). In current study, the overall mortality rate among children with SE was 13 per 100. The studies from developed countries reported mortality between 9–24%.<sup>16,17</sup> Morbidity and mortality from status epilepticus seems to be related to three factors: CNS damage due to the underlying illness or acute insult causing the status epilepticus, CNS damage caused by repetitive electrical discharge of the seizure itself and Systemic and metabolic factors related to repeated Generalized tonic-clonic seizures (GTCS) type of seizures.<sup>17</sup> The major determinants of fatal outcome identified by Sagduyu *et al.*<sup>19</sup> were increasing age, longer duration of SE before initiating therapy, CNS infection as a cause for SE. These factors correlate well with our study. However, in current study the mortality associated with SE was greatest (46%) in children between 2 to 5 years of age followed by 5 to 10 years (28%), less than 2 years (20%) and in children between 10 to 12 years of age (6%). This age difference was statistically significant with p value of 0.039. Proper prehospital therapy, early referral, proper care while transporting, anticipating risk factors involved, and

protocol based approach uniformly at all hospital can reduce the mortality due to status epilepticus in children. Also considering the large number of referrals, upgradation of intensive care facilities even in tertiary care hospital is much sought to improve the overall outcome of SE.

## CONCLUSION

Seizures are not only the cause of high morbidity and mortality in children but also are the reasons of physical, mental and financial distress for their parents. Male preponderance and younger age at presentation were the highlights. The commonest type of seizure was a generalised tonic-clonic seizure. Seizure disorder, acute CNS infections, and febrile seizures were commonest etiological. A good clinical evaluation and if required CSF analysis, Neuroimaging and EEG have the important role in diagnosis. We suggest a long term follow-up study in patients with seizures with regards to their neuro-behavioral outcomes.

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