

**Original article****The Status Epilepticus in Adults: Results from a Tertiary Care Teaching Hospital in Karachi, Pakistan**

Shahneela Tabassum,<sup>1</sup> Munawar Hussain Soomro,<sup>2</sup> Aijaz Ali,<sup>3</sup> Imran Ahmed,<sup>4</sup> Sehrish Shafique,<sup>5</sup> Mujeeb ur Rahman,<sup>6</sup> Shahnaz Shah,<sup>7</sup> Tariq Feroz Memon,<sup>8</sup> Muhammad Munwar Ali,<sup>9</sup> Salma Memon<sup>10</sup>

**Abstract**

**Background:** Status epilepticus is one of the common neurological emergencies associated healthcare costs, morbidity and mortality worldwide. The prevalence is more in extreme ages, in adults as well as in children. However, it can occur at any age. **Aim:** The aim of this study was to determine the possible causes and outcomes of status epilepticus in adults. **Method:** Across-sectional study was conducted in the department of Neurology, at Jinnah Postgraduate Medical College, Karachi during January 2015 to March 2016. All patients of either gender between 18-60 years of age diagnosed for status epilepticus, presented within 24 hours of their first episode of status epilepticus were included in the study. Patients were examined for the assessment of nature, type and presence or absence of precipitating factors (noncompliance, systemic infection, head trauma and central nervous system infections). Data was entered and analyzed by using SPSS version 19.0. **Results:** A total number of 241 patients were recruited. We observed that the patients with no previous history of epilepsy 41(17%) had central nervous system infections, followed by head trauma 27(11%), systemic infections 22(9%) and 3(1.2%) were stroke. In patients who were known case of epilepsy 70(29.0%) patients were found non-compliant to Anti-Epileptic Drug while 30(12.4%) patients were found to have hyponatremia. In 48(19.9%) patients no obvious cause was found. **Conclusion:** Status epilepticus is not common in our setup and predominant type is convulsive status and none of our patients have non convulsive status. Most common precipitating factor was infections followed by trauma. Further studies of bigger dimension are needed to substantiate these findings.

**Keywords:** Status Epilepticus; trauma;adults; Pakistan

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**Introduction**

Status Epilepticus (SE) is considered as one of the most common neurological emergencies associated with morbidity, mortality as well as considered as

costly in terms of healthcare. SE requires immediate steps to follow for prevention and to avoid permanent damage to the brain tissues. In Europe it has been observed that the overall annual incidence of 10–

1. Shahneela Tabassum, Bahria University Medical and Dental College, Karachi, Pakistan. Email: shahneelamujeeb@yahoo.com
2. Munawar Hussain Soomro, Department of Paediatrics, Cumming School of Medicine, and Owerko Centre, Alberta Children's Hospital Research Institute, University of Calgary, Calgary, Alberta, Canada. Email: munawar\_soomro@hotmail.com
3. Aijaz Ali, Department of Neurology, Chandka Medical College and Hospital, SMBB Medical University, Larkana, Pakistan. Email: draijazabbasi28@hotmail.com
4. Imran Ahmed, Bahria University Medical and Dental College, Karachi, Pakistan. Email: drimran72@yahoo.com
5. Sehrish Shafique, Bahria University Medical and Dental College, Karachi, Pakistan. Email: drsehrish80@yahoo.com
6. Mujeeb ur Rahman, Department of Medicine, PNS Shifa, Karachi, Pakistan. Email: surgltmujeebpn@yahoo.com
7. Shahnaz Shah, Department of Neurology, Jinnah Sindh Medical University, Karachi, Pakistan. Email: Shahnaz.shah@jsmu.edu.pk
8. Tariq Feroz Memon, Department of Community Medicine, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan. Email: drtariqferoz@gmail.com
9. Muhammad Munwar Ali, Department of Neurosurgery, Chandka Medical College and Hospital, SMBB Medical University, Larkana, Pakistan. Email: munwardr@yahoo.com
10. Salma Memon, Sindh Education Department, Hyderabad, Pakistan. Email: salmamamnai@gmail.com

**Correspondence:** Munawar Hussain Soomro, Department of Paediatrics, Cumming School of Medicine, and Owerko Centre, Alberta Children's Hospital Research Institute, University of Calgary, Calgary, Alberta, Canada. Email: [munawar\\_soomro@hotmail.com](mailto:munawar_soomro@hotmail.com)

41/100,000 and up to 287,000 patients per year are affected.<sup>1-3</sup>

The term SE is described as a prolonged seizure activity that persists for a long duration of time or repeated enough to produce a fixed and enduring condition. In 2016 International League Against Epilepsy (ILAE) updated definition and has started a five-minute definition so as to emphasize on emergency of condition and to avoid grave consequences if not treated urgently.<sup>4,5</sup> SE is the most serious form of epilepsy and could be due to acute and life-threatening Central Nervous System (CNS) disorder, such as stroke, CNS infection, or head trauma. It has been reported that the mortality associated with SE is up to 20% and less than 50% of patients with SE have had previous seizures or epilepsy.<sup>6</sup> Most often, status is triggered by epilepsy itself including medication non-adherence, inappropriate drug use or drug combination which results in sub-therapeutic Anti-Epileptic Drug (AED) levels.<sup>6</sup>

Cause for SE includes the anti-epileptic drug withdrawal, electrolytes imbalance but often it is not identified, even after complete investigation.<sup>7</sup> Studies from Asian countries have identified different factors leading to SE, i.e., non-compliance (9%), trauma (6%), systemic infection (8%) and fever (10%).<sup>8,9</sup> It is unfortunate that we have no local data of our own on the precipitating factors of SE in our population. There are few studies with limited sample size and in pediatric populations. As per our understanding it is the first of its kind in Pakistan from a tertiary care center in south of Pakistan covering two provinces i.e. Sindh and Baluchistan. The results of this study would provide the frequency of precipitating factors of status epilepticus and further be helpful to clinicians dealing with such cases in emergency and Intensive Care Unit (ICU) setup and strategies would be planned in future which would reduce chances of morbidity and mortality.

### Materials & methods

A cross-sectional study was conducted in the department of Neurology, at Jinnah Postgraduate Medical College (JPMC) Karachi from 1<sup>st</sup> of January 2015 to 31<sup>st</sup> of March 2016. All patients of either gender between 18-60 years of age diagnosed for status epilepticus, presented within 24 hours of their first episode of status epilepticus in emergency department of Neurology were included in the study. All patients who do not meet the criteria by definition, lasting less than 30 minutes, pregnant women,

refused to consent or withdrawn from the study were excluded. A non-probability consecutive sampling technique was used to recruit the patients in the study. A total number of 250 patients were included in the study based on inclusion and exclusion criteria. Nine participants withdrawn from the study to participate. Hence, we ended up with 241 participants for the final analysis.

### Data collection

The data was collected from all patients received and registered at indoor and emergency department. Informed written consent in English and Urdu language were developed and were signed by all the participants. A questionnaire was developed and was pilot tested. A detailed history was taken, and examination was conducted for all patients and further they were assessed for precipitating factors like non-compliance, systemic infections, head trauma, stroke, and CNS infection. The ethical approval was received from JPMC Ethical Review Committee before the start of study.

### Data analysis

Data was entered in EpiData for double checks and was analyzed by using SPSS version 22. General demographic information, mean and standard deviation was calculated for age, height, weight, Body Mass Index (BMI). Frequencies and percentages were calculated for gender, educational status, socio-economic status, and precipitating factors. Stratification with respect to age, BMI (underweight, normal, and obese), educational status, socio-economic status and gender was done. P-value less than equal to 0.05 was taken as significant.

### Results

A total of 241 patients were included in this study. The age of the patients ranged from 18-60 years. The average age of the patients was  $36.1 \pm 6.7$  years, mean height was  $161.94 \pm 7.62$  cm, mean weight was  $67.73 \pm 11.92$  kg and mean BMI was  $25.7 \pm 4.05$ . 167(69.3%) were male and 74(30.7%) were female. As per educational status 9(3.8%) were illiterate, 29(12%) were primary educated, 99(41.2%) had secondary education, 69(28.8%) were intermediate Qualified and 35(14.5%) were graduated or above. 123(51%) of them had monthly income less than equal to Pak rupees 20,000, 89(37%) had between 21000-50000 and 29(12%) had greater than 50000 (Table 1).

**Table 1. Demographic characteristics of the study population.**

Characteristics	Number	%
<b>Gender</b>		
Male	167	69.3
Female	74	30.7
<b>Educational Status</b>		
Illiterate	9	3.8
Primary	29	12
Secondary	99	41.2
Intermediate	69	28.8
Graduate and above	35	14.5
<b>Economical Status</b>		
Less than equal to PKR. 20,000	123	51%
Between PKR. 21,000-50,000	89	37%
Greater than PKR. 50,000	29	12%
<b>Status Epilepticus</b>		
Non-Compliance	3	13%
Trauma	27	11%
CNS infection	41	17%
Febrile Seizure	22	9%

In patients previously not known to be epileptic most of the patients with status epilepticus had CNS infection i.e., 41(17%) followed by head trauma i.e., 27(11%), systemic infections i.e., 22(9%) and 3(1.2%) were due to stroke. Among patients who were previously known case of epilepsy the most common cause of status was non-compliance 70(29.0%) followed by hyponatremia 30(12.4%). In 48(19.9%) patients no obvious cause were found labeled as idiopathic.

Among CNS infection further causes are also defined (Table 2), while Head trauma (Acute symptomatic epilepsy) further divided and defined (Table 3).

**Table 2: Causes of CNS Infection:**

CNS Infection	Frequency	Percentage
Bacterial Meningitis	16	39.02%
Encephalitis	10	24.3%
Cerebral malaria	08	19.5%
Tuberculous meningitis	07	17.07%

**Table 3: Causes of Head Trauma (Acute symptomatic Epilepsy)**

Head Trauma	Frequency	Percentage
Subarachnoid Hemorrhage	11	40 %
Subdural Hematoma	09	33.3 %
Intracranial Parenchymal Bleed	07	25.9 %

About 221(91.70 %) patients were found to had generalized tonic clonic seizures (GTCS), which was the most common type of seizure in the study while 20 (8.2%) patients had partial seizure with secondary generalization.

We further stratified the precipitating factors with age, gender, BMI, educational status, and income. We found non-significant results as shown in the tables 4-8.

**Table 4: Stratification of the precipitating factors with respect to age**

Precipitating factors	18-40	>40-60	P-value
Non-Compliance	Yes	3	0.573
	No	177	
Trauma	Yes	21	0.817
	No	159	
CNS infection	Yes	32	0.695
	No	148	
Febrile Seizure	Yes	17	0.99
	No	163	

**Table 5: Stratification of the precipitating factors with respect to Gender**

Precipitating factors		Male	Female	P-value
Non-Compliance	Yes	3	0	0.555
	No	164	74	
Trauma	Yes	17	10	0.449
	No	150	64	
CNS infection	Yes	29	12	0.827
	No	138	62	
Febrile Seizure	Yes	15	07	0.906
	No	152	67	

**Table 6: Stratification of the precipitating factors with respect to BMI**

Precipitating factors		Under Weight	Normal Weight	Obese	P-value
Non-Compliance	Yes	0	3	0	0.200
	No	65	114	59	
Trauma	Yes	05	19	03	0.049
	No	60	98	56	
CNS infection	Yes	06	33	02	0.000
	No	59	84	57	
Febrile Seizure	Yes	05	15	02	0.1091
	No	60	102	57	

**Table 7: Stratification of the precipitating factors with respect to educational status.**

Precipitating factors		Illiterate	Primary	Secondary	Intermediate	Graduate and above	p-value
Non-Compliance	Yes	0	0	02	01	0	1.00
	No	09	29	97	68	35	
Trauma	Yes	01	02	09	07	08	0.246
	No	08	27	90	62	27	
CNS infection	Yes	03	07	19	09	03	0.198
	No	06	22	80	60	32	
Febrile Seizure	Yes	0	01	12	06	03	0.628
	No	0	28	87	63	32	

**Table 8: Stratification of the precipitating factors with respect to Income status**

Precipitating factors		≤20,000	>20,000-50,000	>50,000	P-value
Non-Compliance	Yes	02	01	0	0.770
	No	121	88	29	
Trauma	Yes	19	07	01	0.082
	No	104	82	28	
CNS infection	Yes	27	09	05	0.076
	No	96	80	24	
Febrile Seizure	Yes	16	05	01	0.096
	No	107	84	28	

## Discussion

Status epilepticus (SE) is one of the most common emergencies in neurology department. It has high morbidity and mortality. Refractory SE to first line anticonvulsants is more critical with a very poor outcome.<sup>1,3</sup>

Unfortunately, the definition of SE is still subject to much confusion. The confusion is more among emergency physicians and General physicians who are the first to contact with patients. In some studies, besides failure of anticonvulsants, duration of seizure has been used as the cornerstone of the definition. While in others it has been the failure of a number of anticonvulsants regardless of duration of seizure activity. To resolve this issue ILAE has clarified that for all practical purpose any seizure that does not resolve in five minutes will be treated as status epilepticus. However for research purpose in epidemiological studies 30 minutes definition will be used retrospectively.<sup>3,5</sup> In current study we have also adhered to this definition.

Status has many classifications, but convulsive status epilepticus (CSE) and non-convulsive status epilepticus (NCSE) are the most important clinical types. The diagnosis is difficult on the clinical grounds alone and needs investigation like electroencephalogram (EEG), and prolong EEG monitoring especially in-patients having NCSE.<sup>7</sup>

To identify the predictive and prognostic characteristics associated with SE, we analyzed data of all patients presenting within 24 hours of first episode of SE to emergency department over a period of 15 months. The time duration of status epilepticus were found to be within 30 min to 12 hrs before the patient arrived at hospital emergency room.<sup>7,10</sup>

Males' population constitute the major chunk of our cases and in this regard our findings are in concordance with Bhalla et. al.<sup>11</sup> and like them we also agree that it has social reason to it, males have priority over females in low socioeconomic group as he is the earning member of family and is given priority for treatment over females.

We only found patients with convulsive status epilepticus in our study and there was not a single case of Non convulsive status which is slightly different when compared with data from regional center in Asia, and from international literature. Bhalla et. al.<sup>11</sup> found 2.5% non-convulsive status in their patients but their major chunk of patients were of convulsive status like ours. However the

reason could be multiple including the availability of prolong EEG monitoring in ICU setup which is must to identify this type and this facility is not available routinely in our setup to identify and secondly is the awareness among health care persons dealing with such cases for identification.

We divided type of status based on history by attendants as was primary generalized and in most of the cases followed by secondary generalized. The most common type of seizure noticed at initiation in our study group was generalized tonic-clonic seizure. However, it is possible that focal onset may have not been noticed by the bystanders/relatives, therefore not documented.

Among the precipitating factors our findings were Non-compliance among known epileptics was 29% of cases, hyponatremia was in 12.4 %. In patients who were not known case epilepsy the precipitating factors was CNS infections in 17%, Head trauma (acute symptomatic epilepsy) was in 11%, systemic infections were in 9%, and Stroke was in 1.2 %.

Studies from neighboring region have shown infections as the most common cause in children and drug default in adults. In our study the most common cause is drug noncompliance as it was done in adults. However we need further studies that too in different ethnic groups with a larger data set to resolve this issue.<sup>7,11,12</sup>

In present study total of 241 patients were enrolled among them 148 were known case of epilepsy while 93 patients were presented with SE as a presentation. Among these 93 patients CNS infections, head trauma, systemic infections and stroke (hemorrhagic/ ischemic stroke) found to be the precipitant of SE. In patients who were known case of epilepsy (148 totals) the commonest cause of SE were non-compliance 70 (29%) followed by hyponatremia 30 (12.4%). Precipitating factor could not be traced in 48 (19.9%) patients and the cause of SE labeled as idiopathic.

Systemic and CNS infections are common precipitating causes.<sup>10,13</sup> Intracranial infections were the common cause of status epilepticus in present study. Meningitis was more common than acute viral encephalitis hence the rationale for starting empirical antibiotics therapy in all cases pending investigations in the emergency setup. Among CNS infections (total 41 patients) most common is meningitis 16 (39.02%), followed by encephalitis 10 (24.3%), than cerebral malaria 08 (19.5%), and lastly tuberculous

meningitis in 07 (17.07%).

Our other common cause is acute symptomatic seizures due to head trauma (total 27 patients) which are further divided into subarachnoid hemorrhage 11(40 %), subdural hematoma 09 (33.3%) and intracranial parenchymal bleed 07(25.9 %). Being a tertiary care center and with a well-established neurotrauma unit this figure is not strange to us.

Stroke is one of the causes of symptomatic epilepsy, especially in the elderly age group. The frequency of seizures in stroke ranges between 2.3 to 14%.<sup>10,13</sup> It can be a presenting symptom of a stroke and associated with increased mortality. Both types of strokes (hemorrhagic and ischemic) can result in seizure and SE. In this study, stroke was an important cause of new onset SE.

Clinical as well as experimental data have shown the proconvulsive properties of hyponatraemia.<sup>14</sup> In one study, hyponatraemia within the first 24 hours of onset of SE was significantly associated with poor response to treatment. These patients were on carbamazepine, oxcarbazepine, or other drugs which can cause low serum sodium levels. In this study 30 of our patient was found to have hyponatremia as a cause of status epilepticus.<sup>15</sup> SE is not a cause of low serum sodium levels, although the causal relationship between hyponatraemia and SE is not clear, few studies suggest that correcting hyponatraemia in patients with SE with due consideration of the risk of severe neurological deficits when reloading serum sodium too rapidly.<sup>15,16</sup>

In this study we found poor drug compliance as a most common cause of SE. This finding needs further elaboration as it is a preventable precipitant of SE. In different studies it was shown that poor adherence to AED is associated with a three-fold increased mortality. In another study, low serum level of antiepileptic medications in epileptic patients was the most common etiology of SE.<sup>17</sup> The cause of poor drug compliance with AEDs are costs of medication, risk of side effects of AEDs, casual attitude and forgetting doses, and simultaneous presence of comorbid mood disorders which will make patients depressed and hopeless. Etiology is considered idiopathic if there was no clinical, laboratory or radiological evidence sufficient to support a specific cause.

The demographic features of the study population were similar to a previous retrospective emergency-based study. All patients were older than 18 years; the clinical features are not representative for all

age groups. In the present study, the rate of non-compliance was 1.2% which is lower than the 9% reported by Mayer *et al.*<sup>18</sup> This difference is most likely because of the definitions used and also because of different population. The lack of data on the overall figures of status epilepticus cases and a selection bias might be assumed as only emergency patients are in these studies. Clearly, most of patients with SE will not have entered the emergency department of our hospital as Karachi has numerous other well developed and reputed hospitals and due to source limitations multi-centre studies could not be possible. Therefore, these series of patients might not be representative of patients with SE in general.<sup>15</sup> None of our cases have alcohol or alcohol withdrawal fits.

Stratification of the precipitating factors with respect to BMI (under weight, normal and obese), educational status, economic status and gender was done, and no significant difference were found other than BMI with significance difference with respect to CNS infections and head trauma. The significance of these findings is difficult to conclude as no previous studies available. We need further studies for conclusion.<sup>16</sup>

None of our participants has any of the autoimmune etiology which is now being picked up so frequently and the reasons could be many folds, first of all it was an emerging concept in those days and even health care providers were not familiar with this concept and secondly facility for testing was not available in Karachi at that time but was available in Islamabad only and at a cost not affordable by patients and institution.

We have intentionally not included the management strategies including no of drugs used and duration of stay in Intensive care unit and ventilator support as this will go beyond the domains of objectives.<sup>16,17</sup>

The limitation of this study needs to be considered. The sample size from one healthcare facility is small. We need future multi-centre studies with a larger sample size to enhance the interpretation of results, which will strengthen the conclusions. Despite this limitation, the study gave an insight into the clinical presentation and types and precipitants of status Epilepticus in our setup.

### **Conclusion**

Findings of this study concluded that precipitating factors of status epilepticus from our setup included infections both CNS and systemic followed by acute symptomatic seizures and poor drug compliance.

Recognition of these are important to cover in treatment modalities for better neurological outcome. Further studies of bigger dimension are needed to substantiate these findings.

#### Ethical considerations:

The protocol was approved by ethical approval was received from Jinnah Postgraduate Medical Centre (JPMC) Ethical Review Committee.

**Conflicting interests:** None

#### Authors' contributions:

ST, AB, participated in study design, data entry

and analysis, data interpretation, draft writing and editing. IA, SS, MR, SS, TFM, MMA and SM participated in data interpretation, draft writing and editing. MHS has participated in study design, data analysis, and data interpretation draft writing, editing and submission. All authors read and approved the final manuscript.

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