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Original Article

Internal Medicine Section

Assessing the Role of Status Epilepticus Severity Score in Predicting Outcome in Patients with Convulsive Status Epilepticus: A Cross-sectional Study

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ABSTRACT

Introduction: Status Epilepticus (SE) is a neurological emergency that necessitates prompt intervention and treatment. The Status Epilepticus Severity Score (STESS) is a clinical tool developed to assess the mortality rate among patients diagnosed with Convulsive Status Epilepticus (CSE).

Aim: To assess the accuracy of STESS in predicting the outcome of CSE.

Materials and Methods: This cross-sectional study was conducted at Jawaharlal Nehru Medical College, Aligarh, Uttar Pradesh, India from December 2020 to November 2022, involving 110 patients aged more than 15 years presenting with CSE lasting more than five minutes. Age, gender, seizure type, history of epilepsy, Glasgow Coma Scale (GCS), and STESS at presentation were assessed and associated with the outcome.

Results: Among the 110 patients included in the study, there was a higher number of male patients compared to female patients. The mean age of the patients was 35.77±17.9 years. The most prevalent type of seizure observed was generalised tonic-clonic seizures, accounting for 65.45% of the cases, 9.09% of the patients expired, 89% of the patients had a STESS below 2. The Receiver-Operating Characteristic (ROC) curve for STESS at presentation to predict in-hospital mortality had an area under the curve of 0.859, 95% Confidence Interval (CI) from 0.780 to 0.918, and p-value<0.0001. It had a sensitivity of 70%, specificity of 95%, Positive Predictive Value (PPV) of 58.3%, Negative Predictive Value (NPV) of 96.9%, and diagnostic accuracy of 92.73%.

Conclusion: Assessment of in-hospital mortality at the onset of SE was reliably determined by STESS and is an useful clinical score. To fully comprehend the reasons for the high overall mortality rate following SE and potential prognostic factors, more research is required.

Keywords: Northern India, Outcome assessment, Predictive value

INTRODUCTION

The term "seizure" is derived from the Latin word meaning "to take possession of," and according to the International League against epilepsy, it refers to transient signs and symptoms brought on by aggravated and abnormal neuronal discharges in the brain [1]. It is the most important neurological condition and a major cause of neurological mortality and morbidity. One of the earliest known diseases was first described around 2500 BC, according to historical records [2]. Epilepsy is a neurological condition characterised by the occurrence of recurrent seizures in individuals, which can be attributed to an underlying cause or condition. It ranks as the second most prevalent and frequently occurring neurological disorder [3]. Ninety percent of the 70 million reported cases worldwide originate from developing nations [4]. Data from multiple studies conducted in different regions of India exhibit significant variations in terms of prevalence and incidence [5-8].

CSE can be caused by various factors, including cerebrovascular disease, acute viral encephalitis, alcohol consumption, drug use, withdrawal, low levels of Antiepileptic Drugs (AEDs), brain hypoxia or anoxia, metabolic disturbances, autoimmune diseases, intracranial tumours, head trauma, and genetic abnormalities. While aetiology is the most important predictor of outcome, age and medical co-morbidity are independent risk factors for mortality [9].

The STESS, as described in [Table/Fig-1], was developed by Rossetti AO et al., with the aim of predicting the survival rate of adult patients with SE prior to the commencement of treatment. A score ranging from 0 to 2 is regarded as favourable, signifying a reduced risk of mortality, while a higher score is associated with an unfavourable prognosis. The assessment is predicated upon the evaluation of age, previous seizure history, seizure type, and the degree of impairment in consciousness [9,10].

	Features	STESS
Consciousness	Alert or somnolent/confused	0
	Stuporous or comatose	1
Worst seizure type	Simple partial, complex partial, absence, myoclonic	0
	Generalized-convulsive	1
	Non-Convulsive Status Epilepticus (NCSE) in coma	2
Age (years)	<65	0
	>65	2
History of previous seizure	Yes	0
	No	1
Total		6

[Table/Fig-1]: Status Epilepticus Severity Score (STESS) [9,10].

STESS is not a reliable indicator for predicting overall mortality after discharge, and alternative scores have been developed for extreme age groups [11]. The modified STESS (mSTESS) mitigates the ceiling effect of the STESS for patients aged 65 years and above. Nevertheless, this approach fails to consider the various factors contributing to SE and has not undergone external validation [12]. The Epidemiology-based Mortality Score in Status Epilepticus (EMSE) may appear to be a potential enhancement compared to the STESS [13]. However, it is important to note that EMSE does not assess Non Convulsive Status Epilepticus (NCSE), and the

computational demands associated with its implementation in a clinical environment are relatively challenging [14].

Although prior studies in this region of Northern India have identified clinical, biochemical, and radiological factors linked to unfavourable outcomes in CSE cases, none have compared the association of STESS with the outcome [15,16]. The current study was one of the first in the North Indian region to compare STESS with the outcome. The study aims to assess the individual parameters used in the STESS for predicting the outcome of CSE. Additionally, the study aims to evaluate the predictive accuracy of the STESS as a clinical tool for predicting the outcome in a resource-limited setting in Northern India.

MATERIALS AND METHODS

The study was conducted at the Department of Medicine, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, a tertiary care centre located in Northern India, from December 2020 to November 2022, over a period of two years. The study protocol was approved by the Institutional Ethical Committee (IEC No: IECJNMC/503), and the study was conducted as per the standards of good clinical practice and the Helsinki Declaration.

Inclusion criteria: Patients older than 15 years (those under 15 were referred to the paediatric department of the emergency trauma centre). Patients who presented with convulsive tonic-clonic seizures lasting beyond five minutes or intermittent seizures with impaired consciousness for more than 30 minutes were included in the study.

Exclusion criteria: Patients who presented with acute traumatic seizures, myoclonic epilepsies, psychogenic seizures, seizures secondary to brain tumours, eclampsia, or patients whose attendants refused to give consent were excluded from the study.

Sample size: In a meta-analysis conducted by Fiest KM et al., it was determined that the lifetime prevalence of epilepsy was 7.60 per 1,000 persons (95% CI 6.17 to 9.38) [7]. Considering the above-mentioned prevalence, the authors used the formula

$n=Z^2\times\{p\times(1-p)\}/E^2$,

(where Z is the Z-score corresponding to the desired confidence level, 'p' is the estimated proportion of the population with the attribute of interest, and E is the desired margin of error) to calculate the sample size for this study [17]. A sample size of 108 was established with 95% confidence and a 5% margin of error.

Study Procedure

Patient age, gender, GCS at presentation, history of previous seizures, and family history of seizures were recorded. The seizures observed at presentation were categorised based on Fisher RS et al., classification, including Generalised Tonic-Clonic Seizures (GTCS), Focal to Bilateral Tonic-Clonic Seizures (FBCS), and Uncertain to Tonic-Clonic Seizures (UTCS) [18]. STESS at presentation was recorded. The time interval from seizure till arrival to hospital was also recorded. Each patient received treatment in accordance with the treatment protocol for CSE established by the Department, adapted and modified from the International League against Epilepsy Guidelines [19].

The patients in the study were classified into two groups based on their outcomes: 1) patients who were discharged after the cessation of seizures with or without any remaining neurological impairment caused by complications of CSE or the primary disease; and 2) patients who expired.

STATISTICAL ANALYSIS

The association between age, gender, history of previous seizures, GCS at presentation, and STESS at presentation with mortality was determined. The Independent t-test (for two groups) and the Chi-square test were used to analyse the association between the qualitative variables. Fisher's exact test was applied in cases where any cell had an expected value <5. Receiver Operating Characteristic (ROC) curve analysis was used to find the cut-off point, sensitivity, specificity, PPV, and NPV of STESS at presentation for predicting an unfavourable outcome. The final analysis was carried out using the Statistical Package for Social Sciences (SPSS) software, manufactured by IBM, Chicago, USA, version 25.0, after entering the data into a Microsoft Excel spreadsheet. For statistical significance, a p-value <0.05 was considered statistically significant.

RESULTS

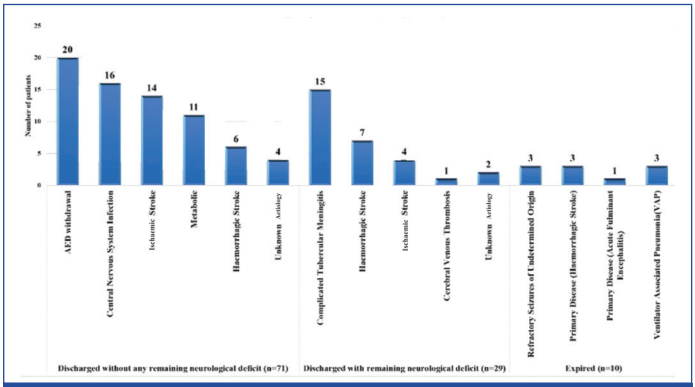
This study included 110 patients diagnosed with CSE, with age ranging from 15 to 75 years. The mean age observed in the study was 35.77±17.9 years. In the present study, 65 (59.09%) were males, while 45 (40.91%) were females. Out of the 110 patients, 20 (18.18%) had a prior history of epilepsy and were prescribed antiepileptic medication. Out of those 20 patients, 16 had a history of non compliance with AEDs, leading to breakthrough seizures. Among the 16 non compliant patients, 12 were discharged, and four expired. Out of the 110 patients, 100 were discharged, and 10 patients expired. The clinical characteristics of the patients in the study are shown in [Table/Fig-2]. Among the 100 discharged

Parameters		n (%)
Age (years)	15-30	56 (50.91)
	31-45	22 (20.00)
	46-60	20 (18.18)
	>60	12 (10.91)
	Mean±SD	35.77±17.9
Gender	Female	45 (40.91)
	Male	65 (59.09)
Family history of epilepsy	Absent	101 (91.82)
	Present	9 (8.18)
History of seizure	Absent	90 (81.82)
	Present	20 (18.18)
Lack of compliance to AED among study participants who were on AED medication (n=20)	No	4 (20.00)
	Yes	16 (80.00)
Type of seizure type in study subjects at presentation	GTCS	72 (65.45)
	UTCS	28 (25.45)
	FBTCS	10 (9.09)
Time interval between onset of seizure and arrival (hours)	<1 hour	18 (16.36)
	1 to 5	28 (25.45)
	6 to 24	59 (53.64)
	>24	5 (4.55)
	Mean±SD	9.11±9.32
Glasgow Coma Scale (GCS) of study subjects	13-15	84 (76.36)
	8-12	16 (14.54)
	3-7	10 (9.09)
STESS at presentation	1	55 (50.00)
	2	43 (39.09)
	3	7 (6.36)
	4	5 (4.55)
Outcome	Discharged without any remaining neurological deficit	71 (64.55)
	Discharged with remaining neurological deficit	29 (26.36)
	Expired	10 (9.09)

[Table/Fig-2]: Clinical characteristics of patients.
GTCS: Generalised tonic clonic seizures; UTCS: Uncertain to tonic clonic seizures; FBTCS: Focal to bilateral tonic clonic seizures; STESS: Status epilepticus severity score; AED: Antiepileptic drugs

patients, 71 were discharged without any remaining neurological deficit or impairment of consciousness, while 29 were discharged with residual neurological deficit or impairment of consciousness.

Aetiology of the patients who presented with CSE is summarised in [Table/Fig-3]. The most common aetiology among patients discharged without any remaining neurological deficit was secondary to AED withdrawal. In patients discharged with remaining neurological deficit, the most common aetiology was complicated tubercular meningitis. Among the 10 patients who expired, three expired due to refractory seizures of undetermined origin, four due to the primary disease, and three due to sepsis resulting from Ventilator-Associated Pneumonia (VAP). The mean length of hospitalisation for patients under study was 8.93±6.26 days.



[Table/Fig-3]: Aetiology of patients under study.

[Table/Fig-4] displays the association between mortality and various factors. It is evident that higher age, UTCS type of seizures, delay in the time interval between seizure onset and arrival, and lower GCS at presentation were all associated with unfavourable outcomes. The association between STESS and outcome was statistically significant. Additionally, the proportion of patients who expired was significantly higher in patients with STESS >2 (58.33%) compared to those with STESS less than or equal to 2 (3.06%) (p-value<0.0001).

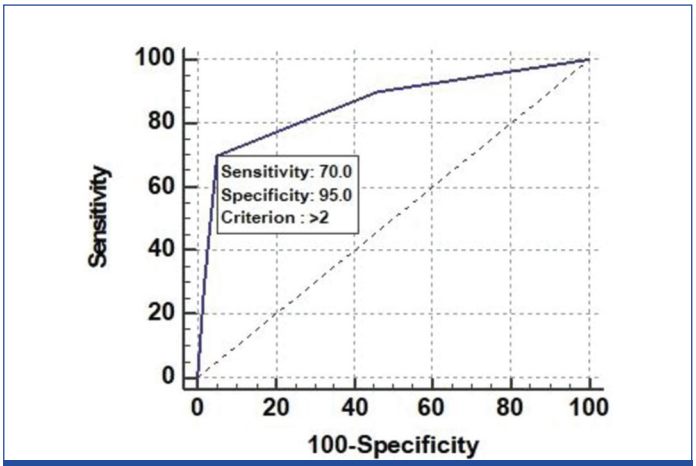
Parameters		Expired (n=10)	Discharged (n=100)	Total (n=110)	p-value
Age (years)	Mean±SD	46.7± 13.89	34.68± 17.94	35.77± 17.9	0.042‡
Gender	Female	5	40	45	0.54†
	Male	5	60	65	
Seizure type	FBTCS	0	10	10	0.0008*
	GTCS	2	70	72	
	UTCS	8	20	28	
Family history of epilepsy	Present	0	9	9	1*
	Absent	10	91	101	
AED therapy non-compliance	Yes	4	12	16	0.037*
	No	6	88	94	
History of epilepsy	Absent	10	80	90	0.203*
	Present	0	20	20	
Time interval between onset of seizure and arrival (hours)	Mean±SD	15.4± 9.92	8.48± 9.08	9.11± 9.32	0.025‡
Glasgow Coma Scale (GCS)	Mean±SD	7.1± 3.7	13.54± 2	12.95± 2.87	0.0003‡
STESS at presentation	≤2	3 (3.06%)	95 (96.94%)	98 (100%)	<0.0001*
	>2	7 (58.33%)	5 (41.67%)	12 (100%)	

[Table/Fig-4]: Association of factors with mortality.
‡Independent t-test, †Chi-square test, *Fisher's-exact test

Upon analysing the ROC analysis of STESS at presentation for the prediction of mortality with a STESS of more than 2, the Area under the ROC curve (AUC) was 0.859 with a standard error of 0.0736, 95% CI of 0.780 to 0.918, sensitivity (95% CI) of 70% (34.8-93.3%), specificity (95% CI) of 95% (88.7-98.4%), PPV (95% CI) of 58.3% (27.7-84.8%), and NPV (95% CI) of 96.9% (91.3-99.4%) [Table/Fig-5,6].

Mortality	STESS at presentation
Area under the ROC curve (AUC)	0.859
Standard error	0.0736
95% Confidence Interval (CI)	0.780 to 0.918
p-value	<0.0001
Cut-off	>2
Sensitivity (95% CI)	70% (34.8-93.3%)
Specificity (95% CI)	95% (88.7-98.4%)
PPV (95% CI)	58.3% (27.7-84.8%)
NPV (95% CI)	96.9% (91.3-99.4%)
Diagnostic accuracy	92.73%

[Table/Fig-5]: STESS at presentation for predicting mortality.



[Table/Fig-6]: Receiver operating characteristic curve of STESS at presentation for predicting mortality.

DISCUSSION

The purpose of this study was to assess individual parameters used in STESS for predicting the outcome of CSE. Comprehensive information about patients who present with CSE and the variables that affect CSE outcomes is scarce. In the present study, a significant proportion of the patients were between the age range of 15 to 30 years 56 (50.91%). The mean age of the patients included in the study was 35.77±17.9 years. When comparing the association of age with mortality, the mean age of patients who expired was 46.7±13.89 years, which was significantly higher compared to patients who expired at 34.68±17.94 years (p-value=0.042). The current study was consistent with a retrospective observational study conducted by Dani R et al., which reported a statistically significant association between the age of participants and the outcome [20]. Among patients under the age of 40 years, 73.5% had favourable outcomes, while only 47.7% had a favourable outcome among those above the age of 40 {Odds Ratio (OR) 3.05, 95% CI 0.9-9.6}. Rossetti AO et al., reported a significant association of mortality with the age of patients >65 years and reported on multiple logistic regression analysis on mortality with age along with potentially fatal aetiology of study subjects and extent of conscious impairment [9]. Other studies conducted by Aukland P et al., and Stelzer FG et al., have reported similar results [11,21].

The percentage of patients who expired in present study was more in patients who had no past history of epilepsy; however, there was

no statistically significant association (p-value=0.203). According to Stelzer FG et al., in their prospective study conducted among 105 patients, 52.4% (n=55) of their study subjects had prior epilepsy. Their study reported a significant association between presence of prior epilepsy and mortality, with 18.18% mortality in patients with a history of epilepsy compared to 56.0% in those with no such history (OR 0.17, 95% CI 0.1-0.4, p-value=0.001) [21].

A significant association was observed between the type of seizure and mortality, with the proportion of patients who expired being significantly more with UTCS compared to FBTCS and GTCS, while the proportion of patients discharged was significantly higher in FBTCS and GTCS compared to UTCS (p-value=0.0008). According to a study by Stelzer FG et al., 28.57% of the patients under study had GTCS, which had a 20% mortality rate (OR 0.34, CI 0.1-0.9), and 14.28% had FBTCS, which had a 26.7% mortality rate (OR 0.5, CI 0.1-2.0) [21]. Huang TH et al., reported that 10.16% of study participants had FBTCS and 33.96% had GTCS, with 33.33% mortality in those who presented with FBTCS [22]. However, there was no statistically significant link between seizure type and mortality (p-value=0.115). Aukland P et al., compared the mortality rates among the various seizure types at presentation and reported a statistically significant association with mortality rates of 48% in patients who presented with GTCS, 24% in patients who presented with complex partial and absence seizures, and 28% in patients who presented with NCSE in a coma (p-value=0.02) [11].

Since our facility provides tertiary care, the majority of patients are referred by primary and secondary care hospitals, which resulted in a significant delay in patient arrival. Only local patients could arrive at our facility within six hours; the average T1 for the study participants was 9.11±9.32 hours. The mean time between the start of the seizure and arrival (T1) in patients who expired was 15.4±9.92 hours, which was noticeably longer than the 8.48±9.08 hours for survivors (p-value= 0.025). Longer hospital latency was associated with the progression of epileptogenesis and negative outcomes, according to previously reported studies [20,23].

Present study compared the mean GCS of patients with and without mortality and observed a similar difference, with the mean GCS in patients who survived being significantly higher than that of patients who expired (7.1±3.7) (p-value=0.0003). Low GCS may result from a primary disease or reflect anoxic brain damage brought on by prolonged seizures. Rossetti AO et al., compared subjects' levels of consciousness to their mortality and reported a significant correlation between mortality and the extent of consciousness impairment (OR 3.03, CI 1.05 to 11.3, p-value=0.04), with similar observations reported by Aukland P et al., Drislane FW et al., and Neligan A and Shorvon SD [11,24,25].

When comparing the association between STESS and mortality of patients at presentation in pressent study patients, the proportion of patients who expired was significantly higher in patients with STESS >2 (58.33%) compared to STESS of ≤2 in patients who were discharged (p-value<0.001). Millán Sandoval JP et al., conducted an ambispective observational study in 395 patients to validate the STESS characteristics in the Columbian population to predict mortality in SE patients [26]. According to their study, 42.8% of patients had a STESS of more than or equal to 3, and none of the study participants expired with a STESS of 0. ROC analysis of STESS with outcome in their study reported that a STESS of more than or equal to 3 was associated with a poor outcome {sensitivity 84.9% (95% CI 73.9%-92.5%), specificity 65.7% (95% CI 60.2%-70.8 %), positive likelihood ratio 2.5 and negative likelihood ratio of 0.2}. Aukland P et al., reported a significant association of STESS with mortality, with 79% mortality in patients with a STESS of more than or equal to three and 95% mortality in patients with a STESS of more than or equal to four (p-value=0.001) [11]. Their study reported that STESS at the onset of SE reliably assessed in-hospital mortality and was indicative of overall survival.

Limitation(s)

There were a number of limitations in the present study. Firstly, the study was conducted exclusively at a single centre located in Northern India. Consequently, the results may not be applicable to other healthcare settings or regions characterised by distinct demographics and healthcare practices. Secondly, there was a lack of follow-up. Lastly, there was no comparison made between the STESS score and other well-established SE scores, such as the modified STESS and EMSE. The analysis conducted by the study may not account for all possible confounding factors that might impact the association between STESS scores and outcomes in patients with CSE.

CONCLUSION(S)

A STESS of more than two was significantly associated with poor outcomes and prompt intervention, especially in a resource-limited setup. The treating physician's clinical judgment should always come first and this score should not be used to rationalise withdrawal of SE treatment. To enhance the predictive accuracy of STESS, it is recommended to undertake prospective validation studies. This can be achieved by extending the study duration to allow for longitudinal follow-up. Additionally, conducting subgroup analyses can be employed to evaluate the performance of STESS across various patient groups. Furthermore, comparing STESS with other prognostic tools, integrating biomarkers or imaging modalities, assessing its impact on treatment decisions and cost-effectiveness, validating its performance in diverse healthcare settings, and developing educational initiatives for healthcare providers are also recommended.

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