Factors associated with poor discharge status in patients with status epilepticus at Khon Kaen Hospital

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Background: Status epilepticus (SE) is a serious neurological condition and has high a mortality rate. Data on importance of factors associated with poor outcomes in Asian or Thai populations are limited.

Methods: Adult patients diagnosed as SE at Khon Kaen Hospital, Thailand from October 1, 2010 to September 30, 2012 were enrolled. Patients were categorized as good or poor outcomes at discharge. Good outcomes were defined by improvement at discharge and absence of neurological deficits, while poor outcomes were defined by: not being improved at discharge; being discharged against advice; death; or presence of a neurological deficit. Clinical factors were compared between both groups.

Results: During the study period, there were 211 patients diagnosed as SE. Of those, 130 patients were male (61.61%). The mean age of all patients was 53.28 years. Acute stroke was the most common cause of SE in 33 patients (15.64%). At discharge, there were 91 patients (43.13%) who had poor outcomes. Only initial plasma glucose levels were significantly associated with poor outcomes with an adjusted odds ratio of 1.012 (95% confidence interval of 1.003 and 1.021).

Conclusion: Initial plasma glucose is associated with poor discharge status in patients with SE.

Keywords: hyperglycemia, outcomes, prognosis, risk factors

Introduction
Status epilepticus (SE) is an emergency neurological condition defined as a continuous seizure of more than 5 minutes.1 Its prevalence varies between 10 and 41 cases per 100,000 population outside of Thailand.2 In Thailand, SE occurred in 5.10 cases per 100,000 population with a mortality rate of 0.6 per 100,000 population.3 Causes of SE are different between countries. A report from Taiwan showed that central nervous system infection and previous strokes are the two most common causes of SE,4 while antiepileptic drug (AED) withdrawal and alcohol-related causes were leading causes of SE in Western countries.5

Factors associated with poor outcomes of SE were related to comorbid complications such as metabolic disorders, cerebrovascular disease, and hypoxemia as shown in systematic reviews.6,7 A report from Thailand did not find any significant predictors for SE.2 Unlike in Western countries, there are limited data on predictors of SE outcomes in Thailand and other Asian countries. Here, the study was aimed to determine whether any factors associated with initial laboratory findings or treatment of SE had influences on outcomes at discharge.
Materials and methods
This study retrospectively reviewed charts of adult patients who were at least 15 years old and diagnosed as SE at Khon Kaen Hospital from October 1, 2010 to September 30, 2012. SE patients were identified by using the International Classification of Diseases code G41. Khon Kaen Hospital is the tertiary care hospital located in the northeastern part of Thailand.

Baseline characteristics, initial laboratory findings, treatment, and treatment outcomes were recorded. Patients were categorized into two groups by type of discharge status and neurological outcomes; good or poor outcomes. Good outcomes were defined by improvement at discharge and absence of neurological deficits, while poor outcomes were defined by: not being improved at discharge; being discharged against advice; death; or presence of a neurological deficit.

Statistical analysis
Descriptive statistics were used to detect significant differences between patients with good and poor outcomes. Univariate logistic regression analysis was applied to calculate the crude odds ratios (ORs) of individual variables for having poor outcomes. All variables with \( P < 0.20 \) in univariate analysis were included in subsequent multivariate logistic regression analysis. The final model was composed of factors associated with poor outcomes. Analytical results are presented as adjusted ORs, and 95% confidence intervals.

The study protocol was approved by an institutional review committee, Khon Kaen University (HE 561217).

Results
During the study period, there were 211 patients diagnosed as SE. Of those, 130 patients were male (61.61%). The mean age (standard deviation [SD]) of all patients was 53.28 years (15.92). Epilepsy (24.64%) and hypertension (23.22%) were the two most common comorbid diseases. Generalized tonic–clonic seizure was the most common type of SE (179 patients; 94.71%). Acute stroke was the most common cause of SE in 33 patients (15.64%). Other common causes of SE are shown in Table 1. The mean (SD) numbers of AEDs used were 2.05 (1.56) and the mean (SD) length of stay was 5.12 days (6.75). There were 104 patients (49.29%) who developed complications after SE and the most common complication was aspiration pneumonia (53 patients; 25.12%).

At discharge, there were 120 patients (56.87%) who had good outcomes, while 91 patients (43.13%) had poor outcomes categorized by: death (29 patients; 13.74%); not improved or discharged against advice (55 patients; 26.07%); and presence of neurological deficits (7 patients; 3.32%). Most clinical factors at initial presentation were comparable between those who had good and poor outcomes at discharge (Tables 2 and 3). Those who had poor outcomes had more SE occurrences in hospital (30.77% versus 26.07%); and presence of neurological deficits (7 patients; 3.32%); and presence of neurological deficits (7 patients; 3.32%). Most clinical factors at initial presentation were comparable between those who had good and poor outcomes at discharge (Tables 2 and 3). Those who had poor outcomes had more SE occurrences in hospital (30.77% versus 26.07%); and presence of neurological deficits (7 patients; 3.32%); and presence of neurological deficits (7 patients; 3.32%).

Discussion
This study showed two important findings: poor discharge status of SE in a tertiary care hospital was 43.13% and the discharge status of SE patients was associated with initial
Table 2 Clinical factors at initial presentation of patients with SE categorized by type of hospital discharge

| Factors | Good outcome | Poor outcome | P-value |
|---------|--------------|--------------|---------|
| Male    | 76 (63.33)   | 54 (59.39)   | 0.555   |
| Mean age (SD), years | 52.71 (18.71) | 54.04 (19.58) | 0.655 |
| Comorbid diseases | | | |
| Hypertension | 28 (23.33) | 21 (23.08) | 0.965 |
| Diabetes mellitus | 23 (19.17) | 16 (17.58) | 0.769 |
| Alcoholism | 13 (10.83) | 7 (7.69) | 0.445 |
| Stroke | 27 (22.50) | 20 (21.98) | 0.928 |
| Epilepsy | 31 (25.83) | 21 (23.08) | 0.645 |
| Causes of SE | | | |
| Acute stroke | 22 (18.33) | 11 (12.09) | 0.432 |
| AED withdrawal | 9 (7.50) | 10 (10.99) | 0.381 |
| Alcohol related | 14 (11.67) | 16 (17.58) | 0.223 |
| Cardiac arrest | 11 (9.17) | 7 (7.68) | 0.704 |
| CNS infection | 7 (5.83) | 12 (13.19) | 0.065 |
| Septic encephalopathy | 12 (10.00) | 12 (13.19) | 0.470 |
| Type of SE | | | |
| Generalized tonic–clonic | 103 (95.37) | 76 (93.83) | 0.703 |
| Nonconvulsive | 1 (0.93) | 2 (2.47) | 0.703 |
| Epilepsia partialis continua | 4 (3.70) | 3 (3.70) | 0.703 |
| Place of SE occurrence | | | |
| Home | 106 (88.33) | 55 (60.44) | <0.001 |
| Primary Hospital | 10 (8.33) | 8 (8.79) | <0.001 |
| Khon Kaen hospital | 4 (3.33) | 28 (30.77) | <0.001 |
| History of previous SE | 10 (8.33) | 2 (2.20) | 0.057 |

Notes: Poor outcome: discharge by death, not improved, or discharged against advice. Khon Kaen Hospital is a tertiary care hospital. Data presented as number (percentage) unless indicated.

Abbreviations: AED, antiepileptic drug; CNS, central nervous system; SD, standard deviation; SE, status epilepticus.

Table 3 Physical signs and laboratory findings at initial presentation of patients with status epilepticus categorized by type of hospital discharge

| Factors | Good outcome | Poor outcome | P-value |
|---------|--------------|--------------|---------|
| Body temperature, °C | 37.22 (1.01) | 37.42 (1.26) | 0.219 |
| Systolic blood pressure, mmHg | 138.22 (28.41) | 138.24 (32.72) | 0.996 |
| Pulse rate, bpm | 98.42 (23.40) | 102.44 (24.75) | 0.249 |
| Glasgow coma scale | 9.78 (3.51) | 7.97 (4.01) | <0.001 |
| Endotracheal intubation, n (%) | 67 (58.26) | 58 (65.17) | 0.315 |
| Laboratory results | | | |
| Hematocrit, % | 26.04 (17.53) | 23.83 (17.76) | 0.367 |
| White blood cell count, cells/mm³ | 8,492.60 (6,724.24) | 8,411.43 (7,789.93) | 0.936 |
| Plasma glucose, mg/dL | 159.26 (84.18) | 203.11 (121.93) | 0.006 |
| Blood urea nitrogen, mg/dL | 13.32 (10.69) | 31.09 (36.64) | <0.001 |
| Creatinine, mg/dL | 1.18 (1.26) | 2.01 (1.88) | <0.001 |
| Serum sodium, mEq/L | 135.49 (8.03) | 138.03 (6.57) | 0.034 |
| Serum potassium, mEq/L | 3.57 (0.89) | 3.70 (0.77) | 0.318 |
| Serum chloride, mEq/L | 99.27 (9.09) | 103.30 (7.27) | 0.006 |
| Serum bicarbonate, mEq/L | 22.37 (4.81) | 20.03 (5.82) | 0.037 |
| Serum calcium, mg/dL | 8.44 (0.88) | 8.30 (1.38) | 0.532 |
| Serum phosphate, mg/dL | 3.02 (1.12) | 3.79 (2.27) | 0.037 |
| Total cholesterol, mg/dL | 168.08 (49.37) | 158.87 (57.92) | 0.555 |
| Serum albumin, g/dL | 3.52 (0.66) | 2.73 (0.93) | <0.001 |
| Serum ALT, U/L | 533.67 (61.28) | 147.63 (275.02) | 0.052 |
| Serum AST, U/L | 82.78 (102.35) | 171.36 (205.69) | 0.031 |
| Total bilirubin, mg/dL | 1.04 (0.79) | 1.84 (1.49) | 0.017 |
| Alkaline phosphatase, mg/dL | 111.31 (81.39) | 106.89 (88.13) | 0.857 |

Note: Data presented as mean (standard deviation) unless indicated otherwise.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase.
Table 4: Treatment and treatment outcomes of patients with SE categorized by type of hospital discharge

| Factors                                      | Good outcome N=120 | Poor outcome N=91 | P-value  |
|----------------------------------------------|--------------------|-------------------|----------|
| SE time prior to treatment, minutes          | 150.83 (257.64)    | 159.19 (344.43)   | 0.848    |
| SE treatment time to control SE, minutes     | 88.81 (175.08)     | 191.47 (621.38)   | 0.143    |
| Total SE time, minutes                       | 225.77 (268.90)    | 360.09 (723.49)   | 0.108    |
| Recurrent SE, n (%)                          | 13 (10.83)         | 39 (42.86)        | <0.001   |
| Interictal time, hours                       | 5.54 (12.24)       | 1.16 (6.59)       | 0.001    |
| Numbers of AED use                           | 2.55 (1.71)        | 2.44 (1.35)       | 0.612    |
| Types of AED use                             |                    |                   |          |
| Primary AED                                  |                    |                   |          |
| Diazepam, n (%)                              | 91 (75.83)         | 69 (75.82)        | 0.747    |
| Phenytoin, n (%)                             | 26 (21.67)         | 21 (23.08)        | 0.747    |
| Sodium valproate, n (%)                      | 3 (2.50)           | 1 (1.10)          | 0.747    |
| Secondary AED                                |                    |                   |          |
| Phenytoin, n (%)                             | 91 (98.91)         | 77 (100)          | 0.359    |
| Sodium valproate, n (%)                      | 1 (1.09)           | 0                 | 0.359    |
| Others                                       |                    |                   |          |
| Midazolam, n (%)                             | 0                  | 3 (0.03)          | 0.079    |
| Propofol, n (%)                              | 0                  | 2 (0.02)          | 0.185    |
| Length of hospital stay, days                | 4.69 (6.12)        | 5.69 (7.50)       | 0.287    |
| Duration of respirator use, days             | 1.83 (3.92)        | 4.18 (6.21)       | <0.001   |
| Aspirated pneumonia, n (%)                   | 33 (27.50)         | 20 (21.98)        | 0.360    |

**Note:** Data presented as mean (standard deviation) unless indicated otherwise.

**Abbreviations:** AED, antiepileptic drug; SE, status epilepticus.

plasma glucose levels. An increase of 1 mg/dL of plasma glucose increased the risk of having poor discharge status by 1.2%.

A previous study from Singapore also showed that in SE patients with a hyperglycemia equal to or more than 7 mmol/L (126 mg/dL), these levels were associated with poor outcomes of SE. In animal models, hyperglycemia causes hippocampal damage and also aggravates seizures. Therefore, glucose control may be important in SE patients, particularly in Asian populations. These results may not apply to Western populations. Two studies from Switzerland did not have findings similar to this study. Hyperglycemia was, however, shown to be associated with poor outcome in acute ischemic stroke.

Some factors such as serum albumin or aspartate aminotransferase were significantly different between the good and poor SE outcomes by univariate logistic analysis or descriptive statistics. Both factors, however, were not statistically significant in the multivariate logistic regression analysis. These results implied that only plasma glucose was an independent factor or predictor for SE outcome.

The population of this study may be different from other previous studies in terms of causes of SE. In the current study, acute stroke, alcohol related causes, and septic encephalopathy accounted for 41.23% of the entire subjects. Unlike in Western populations, AED withdrawal was found only in 9%. The previous study from Thailand found that the mortality rate of SE was 35%, while refractory SE may have a mortality rate of 50%. The poor outcome rate of this study was 43.13%. The poor discharge statuses were one of the following: death; not improved or discharged against advice; or presence of a neurological deficit.

The strengths of this study were the quite-large sample size and different causes of SE as compared with previous studies. There are some limitations. Retrospective data collection may not have complete data, particularly laboratory findings such as HbA1c levels or history of previous medications that may affect plasma glucose levels such as steroid use. Also noted was that the population in this study was mostly not refractory SE; only three and two patients had received midazolam and propofol, respectively. Further studies are needed particularly in refractory SE. The results of this study may apply only to Asian populations or other countries in Southeast Asia.

**Conclusion**

Initial plasma glucose is associated with poor discharge status in patients with SE.

**Acknowledgments**

This study was supported by TRF grants from Senior Research Scholar Grant, Thailand Research Fund grant number...
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RTA5580004 and the Higher Education Research Promotion and National Research University Project of Thailand, Office of the Higher Education Commission, Thailand through the Health Cluster (SHeP-GMS), Khon Kaen University. The authors also would like to thank Dr Thanachai Panaput for his kind advice on statistical analyses, Ms Kanokwan Boonpracheon (medical student) for her assistance in data management, and Professor James A Will (University of Wisconsin, Madison, WI, USA) for review of the manuscript.

Disclosure
The authors report no conflicts of interest in this work.

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