RESEARCH PAPER

Serum S100B Protein and Neuron Specific Enolase as Biomarkers for Neuronal Injury in Children with Status Epilepticus

Shiamaa Mostafa Elmashad [1*], Tarek Elgohary [1], Sahar Abd Elaziz [1], Hesham Elserogy[2]

1. *1 Pediatrics Department, Faculty of Medicine, Tanta University, Tanta, Egypt*
2. *2 Clinical Pathology Department, Faculty of Medicine, Tanta University, Tanta, Egypt*

Received: 04th June, 2026; Revised: 25th June, 2026; Accepted: 05th July, 2026; Available Online: 20th July, 2026

ABSTRACT

Background/Aim: Convulsive status epilepticus (CSE) is a neurological emergency associated with substantial morbidity and mortality. Prolonged seizure activity may result in neuronal injury, highlighting the need for reliable biomarkers that reflect the extent of brain damage. Neuron-specific enolase (NSE) and S100 calcium-binding protein B (S100B) have emerged as promising peripheral biomarkers of neuronal injury. Although several studies have evaluated NSE and S100B in neurological disorders, evidence regarding their clinical utility in pediatric CSE remains limited. Furthermore, relatively few studies have investigated the relationship between these biomarkers, seizure duration, and treatment requirements in children with idiopathic CSE. Therefore, the present study aimed to evaluate serum concentrations of NSE and S100B in children with CSE and to investigate their association with seizure duration and the number of antiseizure medications required for seizure control.

Methods: This cross-sectional analytical study included 50 children aged 1–16 years with idiopathic CSE and 30 age and sex -matched children with controlled idiopathic epilepsy serving as controls. Serum NSE and S100B concentrations were measured one hour and 24 hours after seizure onset in patients and once in controls using enzyme-linked immunosorbent assay (ELISA). Correlations between biomarker levels, seizure duration, and the number of antiseizure medications required to terminate seizures were analyzed.

Results: Serum NSE and S100B concentrations were significantly higher in children with CSE than in controls ($P < 0.001$). Both biomarkers increased significantly from one hour to 24 hours after seizure onset ($P < 0.001$). No significant differences were observed between generalized and focal CSE. Serum NSE and S100B levels demonstrated significant positive correlations with seizure duration and the number of antiseizure medications required for seizure control ($P < 0.05$).

Conclusion: Serum NSE and S100B levels are significantly elevated in children with convulsive status epilepticus and correlate with seizure severity and duration. These biomarkers may serve as useful adjunctive indicators of seizure-related neuronal injury. Larger prospective multicenter studies are warranted to validate their role in routine clinical practice.

Keywords: Serum S100 Calcium-Binding Protein B, Neuron Specific Enolase, Neuronal Injury, Convulsive Status Epilepticus, Children.

How to cite this article: Elmashad S.M, Elgohary T, Abd Elaziz S, Elserogy H, Serum S100B Protein and Neuron Specific Enolase as Biomarkers for Neuronal Injury in Children with Status Epilepticus. 2026;16(72s): 343-350. DOI: 10.25258/ijddt.16.72s.38

Source of support: None

Conflict of interest: None

INTRODUCTION

Status epilepticus (SE) is a neurological emergency characterized by prolonged seizures causing neuronal injury, blood–brain barrier (BBB) disruption, and increased mortality [1]. SE is one of the most serious neurological emergencies in both children and adults, requiring immediate recognition and prompt treatment to minimize neurological injury and improve clinical outcomes [2]. The most classification referenced in clinical practice is the International League Against Epilepsy (ILAE), operational classification of seizure types which classify seizures into focal and generalized [3]. According to the ILAE, SE is defined as a condition resulting from either the failure of mechanisms responsible for seizure termination or the initiation of mechanisms leading to abnormally prolonged seizures [4]. Operationally, convulsive SE is considered when a generalized tonic–clonic seizure persists for more than 5 minutes (time point T1), while prolonged seizure activity beyond approximately 30 minutes (time point T2) is associated with an increased risk of permanent neuronal injury, neuronal death, and long-term neurological sequelae [5].

Despite substantial advances in the management of pediatric SE, prolonged seizures remain associated with considerable morbidity and mortality [6]. Experimental and clinical studies have demonstrated that sustained epileptic activity results in excessive glutamate release, excitotoxicity, mitochondrial dysfunction, oxidative stress, neuroinflammation, disruption of the blood–brain barrier, and apoptosis, all of which contribute to neuronal and astroglial injury [7]. The extent of this injury appears to increase with seizure duration and treatment delay, emphasizing the importance of early identification of patients at risk of neurological damage [8].

The diagnosis of convulsive SE is primarily clinical and may be supported by electroencephalography

**Author for Correspondence: shimaaelmashed5@gmail.com*

(EEG), particularly when seizure activity is uncertain or non-convulsive SE is suspected. However, neither clinical assessment nor EEG directly quantifies the degree of neuronal injury. Consequently, there has been growing interest in identifying circulating biomarkers that reflect acute brain damage and may provide objective information regarding disease severity, prognosis, and response to therapy [9].].

Neuron-specific enolase (NSE) is one of the most extensively investigated biomarkers of neuronal injury. It is a glycolytic enzyme predominantly localized within the cytoplasm of neurons and neuroendocrine cells [10]. Under physiological conditions, circulating NSE concentrations remain low because of the integrity of neuronal cell membranes and the blood–brain barrier [11]. Following neuronal damage, NSE is released into the extracellular space and subsequently enters the systemic circulation, making it a potential indicator of acute neuronal injury [12]. Elevated serum NSE concentrations have been reported in several neurological disorders, including traumatic brain injury, hypoxic–ischemic encephalopathy, ischemic stroke, encephalitis, and status epilepticus [13].

S100 calcium-binding protein B (S100B) is a calcium-binding protein predominantly expressed by astrocytes and Schwann cells [14]. Increased serum S100B concentrations reflect astroglial activation or injury and are also considered indicators of BBB disruption [15]. Similar to NSE, elevated S100B levels have been described in various acute neurological conditions and have been associated with the severity of brain injury [16]. Because neuronal and astroglial damage occur simultaneously during prolonged seizures, the combined assessment of NSE and S100B may provide complementary information regarding seizure-induced brain injury [17].

Although several studies have evaluated NSE and S100B in neurological disorders, evidence regarding their clinical utility in pediatric convulsive status epilepticus remains limited and sometimes inconsistent [18]. Differences in patient populations, seizure etiology, sampling time, and laboratory methodology have contributed to variable findings across published studies [19]. Furthermore, relatively few studies have investigated the relationship between these biomarkers, seizure duration, and treatment requirements in children with idiopathic convulsive SE [20].

Therefore, the present study aimed to evaluate serum concentrations of neuron-specific enolase (NSE) and S100 calcium-binding protein B (S100B) in children with convulsive status epilepticus and to investigate their association with seizure duration and the number of antiseizure medications required for seizure control. We hypothesized that prolonged seizure activity would be associated with higher serum concentrations of both biomarkers, reflecting increased neuronal and astroglial injury.

PATIENTS AND METHODS:

This cross-sectional analytical study was conducted at the Pediatric Department, Tanta University Hospitals, Egypt, between July 2022 and July 2023. The study enrolled 50 consecutive children aged 1–16 years who presented with idiopathic convulsive status epilepticus (CSE). CSE was diagnosed according to the ILAE criteria as continuous convulsive seizure activity lasting ≥5 minutes or recurrent convulsive seizures without recovery of consciousness between episodes. These patients had been allocated into two groups depending on the seizure type, one group had generalized convulsive SE and the other group had focal SE. The control group comprised 30 age-, and sex -comparable children with previously diagnosed idiopathic epilepsy who had remained seizure-free for at least three months while receiving suitable antiseizure medication therapy. The study protocol was approved by the Institutional Research Ethics Committee of Tanta University Hospital (Approval Code. 34140/9/20), and written informed consent was obtained from the parents or legal guardians of all participants before enrolment.

Inclusion criteria:

Children were eligible if they: were between 1 and 16 years of age; had idiopathic convulsive status epilepticus (generalized or focal motor); and had no evidence of structural brain abnormalities on neuroimaging.

Exclusion criteria:

Children were excluded if they had: non-convulsive status epilepticus; febrile status epilepticus; psychogenic nonepileptic seizures; intracranial infection; acute ischemic or hemorrhagic stroke; traumatic brain injury; brain tumors; inflammatory or demyelinating neurological diseases; neurodegenerative disorders; metabolic encephalopathy; congenital or acquired cardiac disease.

All patients were subjected to complete history taking, thorough clinical examinations, laboratory investigations (routine and research work) and neurodiagnostic evaluation.

Clinical assessment:

All patients underwent comprehensive history taking and physical examination upon admission. The following data were recorded: age and sex; seizure type (generalized or focal); seizure duration; precipitating factors; number of antiseizure medications required for seizure termination; neurological examination findings. The cessation of seizures was ascertained by the enhancement of muscular tone, eye movements, color of the face and light reflex.

Laboratory investigations:

Blood sampling

For children with CSE, 2 venous blood samples each about 5 ml was withdrawn from each child under complete aseptic precautions at two predefined time points. The first sample after one hour from the onset of SE, the other after 24 hours from the onset of SE. For control group, one sample was enough. The blood was collected in plain tubes and allowed to clot then centrifuged for 15 minutes and the serum samples have been separated from the clot within 60 minutes after collection to prevent the leakage of NSE from blood cells.

Immediate assay for **routine laboratory investigations** was done and included: liver function tests, kidney function tests, random blood glucose, serum sodium, serum potassium, ionized calcium, magnesium, phosphorus and antiepileptic drug serum levels. Also, immediate assay for complete blood count was done utilizing EDETA-Collected sample. While the remaining portion of the sample was kept at -20 c until the time of biomarker analysis (NSE and S100B protein). Another arterial blood sample about 0.5 ml was taken through a heparinized syringe for measurement of ABG.

Research biomarkers investigations:

Measurements of serum NSE and S100B

Serum concentrations of neuron-specific enolase (NSE) and S100 calcium-binding protein B (S100B) were quantified using commercially available enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturers' instructions. Calibration curves were generated for each assay, and biomarker concentrations were calculated from the corresponding standard curves. All measurements were performed under identical laboratory conditions. ELISA kits used for NSE and S100B assay were Human NSE ELISA Kit, SunRed, China, 201-12-0938 and Human S100B ELISA Kit, Sun Red, China,201-12-4851, respectively.

Neurodiagnostic evaluation:

Brain magnetic resonance imaging (MRI) was performed to exclude structural brain lesions including tumors, abscesses, prior strokes, or mesial temporal sclerosis.

Electroencephalography (EEG) was carried out after stabilization to confirm epileptic activity, classify seizure type, and exclude alternative diagnoses when clinically indicated.

Outcome measures:

The primary outcome was the difference in serum NSE and S100B concentrations between children with convulsive status epilepticus and controls. Secondary outcomes included the association of biomarker concentrations with: seizure duration; seizure type; and number of antiseizure medications required to terminate seizures.

Statistical analysis:

Data were analyzed using IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA).Continuous variables were tested for normality using the Shapiro–Wilk test. Normally distributed variables are presented as mean ± standard deviation (SD), whereas non-normally distributed variables are presented as median and interquartile range (IQR). Comparisons between two independent groups were performed using the independent-samples Student's *t* test or the Mann–Whitney *U* test, as appropriate. Paired comparisons between biomarker levels measured at one hour and 24 hours were performed using the paired *t* test or Wilcoxon signed-rank test. Correlations between serum biomarker concentrations, seizure duration, and the number of antiseizure medications were assessed using Pearson's or Spearman's correlation coefficients according to data distribution. A P value <0.05 was considered statistically significant.

RESULTS:

1-Baseline clinical characteristics of the patient group

Baseline clinical characteristics of the patient group are summarized in **Table 1**. The mean age of children with CSE was 6.68 ± 3.31 years, and males represented 70% of the study population. Generalized CSE was the predominant seizure type, accounting for 76% of cases, whereas focal motor status epilepticus was observed in 24%. The duration of seizures ranged from 30 minutes to 48 hours, and two to five antiseizure medications were required to achieve seizure control.

Table 1: Baseline clinical characteristics of the patient group

		N=50
Age (years)		6.68±3.31
Sex	**Male**	35(70.0%)
	Female	15(30.0%)
Precipitating factors for SE	**Inappropriate AED type**	3(6.0%)
	Missing doses	9(18.0%)
	Unknown	38(76.0%)
EEG	**Focal epileptic activity**	12(24.0%)
	Generalized epileptic activity	38(76.0%)
Type of seizures	**Partial motor seizures**	12(24.0%)
	Generalized convulsive SE	38(76.0%)
The number of antiseizure medications used to control seizures	**2**	13(26.0%)
	3	13(26.0%)
	4	11(22.0%)
	5	13(26.0%)
Duration of SE (hours)		30–48.0

Data is presented as mean ± SD or frequency (%) or range. SE: Status Epilepticus, EEG: Electroencephalogram, AED: Antiepileptic Drug

2-Comparison of serum NSE and S100B between patients and controls

One hour after seizure onset, children with CSE had significantly higher serum NSE concentrations than the control group (19.18 ± 2.35 vs. 12.66 ± 5.07 ng/mL, P < 0.001). Similarly; serum S100B concentrations were significantly higher in patients with CSE (0.44. ±0.18) than in controls (0.13. ±0.22) [P < 0.001], indicating increased neuronal and astroglial injury associated with prolonged seizures. **Table 2**

Table 2: Comparison between mean serum levels of NSE, S100B one hour after the onset of SE in the patient group and its level among the control group

Type of biomarkers	Status epilepticus (n = 50)	Control group (n = 30)	Test	P
NSE (ng/ml)	19.18±2.35	12.66±5.07	t=6.628	**<0.001***
Serum S100B (ng/mL)	0.44. ±0.18	0.13. ±0.22	t=7.026	**<0.001***

*Data is presented as mean ± SD. *: Significant P <0.05. t: Student t-test. NSE: Neuron Specific Enolase, SE: Status Epilepticus, S100B: S100 Calcium-Binding Protein B*

3-Temporal changes in biomarker concentrations:

Within the CSE group, serum concentrations of both biomarkers increased significantly between the first and second sampling times. Mean serum NSE increased from 19.18 ± 2.35 ng/mL at one hour to 24.54 ± 4.05 ng/mL at 24 hours (P < 0.001).Likewise; serum S100B concentrations were significantly higher at 24 hours (0.72. ±0.36) than at one hour (0.44. ±0.18) after seizure onset (P < 0.001). **Table 3**

Table 3: Comparison between mean serum levels of NSE and S100B one hour and 24 hours following the onset of status epilepticus in the patient group

Type of biomarkers	1 Hour	24 Hours	Test	P
NSE (ng/ml)	19.18±2.35	24.54±4.05	t=13.257	**<0.001***
S100B (ng/mL)	0.44. ±0.18	0.72. ±0.36	t=6.371	**<0.001***

*Data is presented as mean ± SD or range. *: Significant P <0.05. t: Paired t-test. NSE: Neuron Specific Enolase, S100B: S100 Calcium-Binding Protein B*

Biomarker levels according to seizure type:

No statistically significant differences were observed in serum NSE or S100B concentrations between children with generalized convulsive status epilepticus and those with focal motor status epilepticus at either sampling time (all P > 0.05), suggesting that biomarker elevation was associated with prolonged seizure activity rather than seizure semiology. **Table 4**

Table 4: Comparison between mean serum levels of NSE and S100B one hour and 24 hrs after the onset of status epilepticus in the patient group according to to seizure type

Time of mean serum levels	Focal motor SE (n= 12)	Generalized convulsive SE (n= 38)	Test	P
NSE (ng/ml)				
1 Hour	20.12±3.13	18.89±2.01	t=1.286	0.219
24 Hour	25.84±4.30	24.13±3.94	t=1.282	0.206
S100B (ng/mL)				
1 Hour	0.44±0.18	0.68±0.49	t=0.028	0.978
24 Hour	0.68±0.49	0.73±0.31	t=0.355	0.728

Data is presented as mean ± SD. t: Student t-test. NSE: Neuron Specific Enolase, S100B: S100 Calcium-Binding Protein B

5-Correlation between serum biomarkers levels and clinical severity as assessed by seizure duration and the number of antiseizure medications required to terminate seizures:

Serum concentrations of both NSE and S100B showed significant positive correlations with seizure duration. Higher biomarker concentrations were associated with longer seizure duration, indicating greater neuronal injury in children experiencing prolonged convulsive status epilepticus. Furthermore, both biomarkers demonstrated significant positive correlations with the number of antiseizure medications required to terminate seizures. Children requiring multiple antiseizure medications had significantly higher serum NSE and S100B concentrations, suggesting that elevated biomarker levels may reflect increased seizure severity and treatment refractoriness. **Table 5 and Figure 1**

Table 5: Correlation between biomarker serum levels (NSE, S100B), duration of status epilepticus, and the number of antiseizure medications used to control status epilepticus in patient group

Biomarker serum levels	The number of antiseizure medications used to control SE	
	r	P
NSE (ng/ml)	0.549	**<0.001***
S100 B (ng/ml)	0.660	**<0.001***
	Duration of SE (hours)	
NSE (ng/ml)	0.568	**<0.001***
S100B (ng/ml)	0.418	**0.003***

*r: correlation coefficient. *: Significant P <0.05. SE: Status Epilepticus, NSE: Neuron Specific Enolase, S100B: S100 Calcium-Binding Protein B.*

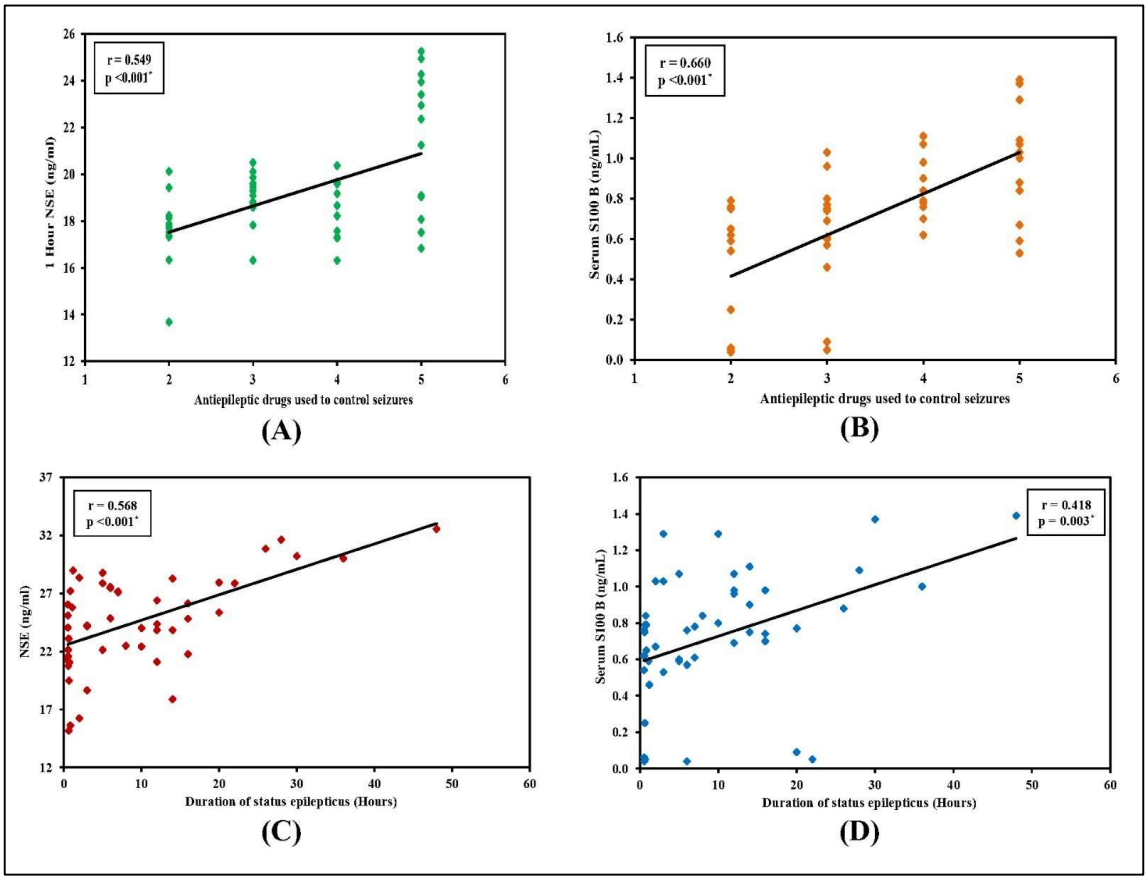

Figure 1: Correlations between biomarker serum levels (neuron specific enolase, S100 Calcium-Binding Protein B), duration of status epilepticus, and the number of antiseizure medications used to control status epilepticus in patient group. A and B correlations between biomarker serum levels and the number of antisezure medications used to control status epilepticus. C and D correlations between biomarker serum levels and duration of status epilepticus.

DISCUSSION:

The present study examined the clinical utility of serum NSE and S100B as biomarkers of neuronal injury in children with idiopathic CSE. We found that serum NSE and S100B concentrations were significantly higher in children with CSE than in those with well-controlled idiopathic epilepsy. In addition, both biomarkers increased during the first 24 hours after seizure onset and showed positive associations with seizure duration and with the number of antiseizure medications required to terminate seizures. No significant differences were observed between generalized and focal CSE. Taken together, these findings suggest that prolonged convulsive seizures are associated with measurable neuronal and astroglial injury and that NSE and S100B may provide complementary information regarding the severity of seizure-related brain injury.

These observations are biologically plausible. Prolonged seizures can induce excitotoxicity, oxidative stress, neuroinflammation, and BBB disruption, all of which may contribute to neuronal damage and astroglial activation [21]. NSE is a glycolytic enzyme predominantly found in neurons and is released into the circulation

following neuronal injury, whereas S100B is mainly produced by astrocytes and is considered a marker of astroglial activation and BBB dysfunction [22]. Because these biomarkers reflect different but related aspects of brain injury, their simultaneous assessment may provide a more comprehensive view of the pathophysiological consequences of prolonged seizures than either marker alone [23].

The higher serum NSE and S100B concentrations observed in this study are consistent with prior evidence linking prolonged seizures to acute neuronal injury. Recent studies have identified both biomarkers among the most promising fluid indicators of neuroglial injury in status epilepticus, although further standardization of assays and prospective validation are still required before routine clinical use can be recommended [24]. Likewise, prospective pediatric studies have reported elevated NSE and S100B concentrations after prolonged seizures, with biomarker levels correlating with seizure severity and clinical outcome measures [25]. Collectively, these data support the biological relevance of our findings and reinforce the potential role of NSE and S100B as adjunctive biomarkers of acute brain injury in pediatric CSE.

The present study demonstrated that serum NSE and S100B concentrations increased significantly between one hour and 24 hours after the onset of CSE, reflecting the dynamic evolution of seizure-induced neuronal and astroglial injury. This temporal pattern is biologically plausible, as neuronal injury continues after seizure termination because of ongoing excitotoxicity, oxidative stress, neuroinflammation, and blood–brain barrier disruption [26]. Accordingly, biomarker measurements obtained during the first 24 hours may better reflect the cumulative extent of brain injury than early single measurements. While NSE represents delayed release from injured neurons, S100B primarily reflects persistent astroglial activation and BBB dysfunction during the early postictal period.

These findings are consistent with those of Cresto , et al [27] who reported progressive increases in both NSE and S100B during the first 24 hours after pediatric CSE, and with the systematic review by Prakash , et al [28], which concluded that serial biomarker assessment is more informative than isolated measurements because neuronal and astroglial injury evolves over time.

Another important finding was the significant positive correlation between serum NSE and S100B concentrations and seizure duration, indicating that longer seizures are associated with greater neuronal injury. This observation is consistent with studies by Wang , et al [29], and Macedo , et al [30], as well as by Lybeck , et al [31], all of them identified seizure duration as one of the strongest predictors of elevated neuroglial biomarkers following status epilepticus.

Serum NSE and S100B concentrations also correlated positively with the number of antiseizure medications required to terminate CSE. Because the need for multiple antiseizure medications reflects greater seizure severity and refractoriness, higher biomarker concentrations most likely indicate a greater burden of seizure-induced brain injury rather than an effect of treatment itself [32]. These findings suggest that NSE and S100B may have prognostic value in addition to reflecting acute neuronal injury, although larger longitudinal studies are needed to determine their ability to predict long-term neurological outcome

Another important finding was the absence of significant differences in serum NSE and S100B concentrations between children with generalized and focal CSE, suggesting that seizure duration and persistence rather than seizure phenotype are the principal determinants of seizure-induced neuronal injury. Similar findings have been reported by Hanin , et al [33], who found that serum NSE concentrations were independent of seizure type after adjustment for seizure duration, while Lange ,et al showed that S100B reflects the severity of neurological injury rather than seizure phenotype [34]. However, the relatively small number of children with focal CSE in our study may have limited the ability to detect modest subgroup differences.

The present findings have important clinical implications. Serum NSE and S100B may serve as complementary biomarkers of seizure-induced brain injury and may assist in assessing disease severity and identifying children at greater risk of prolonged or refractory seizures [35]. However, because these biomarkers are influenced by factors such as BBB disruption and other neurological disorders, they should be interpreted alongside clinical assessment, electroencephalography, and neuroimaging rather than as stand-alone diagnostic tests [36]. The progressive increase in biomarker concentrations during the first 24 hours also supports the value of serial rather than single measurements, although future studies should evaluate additional sampling time points to define their optimal temporal profile.

The strengths of this study include its prospective design, evaluation of two complementary biomarkers, serial measurements at one and 24 hours after seizure onset, and correlation of biomarker concentrations with clinically relevant indicators of disease severity. Nevertheless, several limitations should be acknowledged, including the single-center design, relatively small sample size, inclusion of only idiopathic CSE, absence of cerebrospinal fluid biomarker measurements, limited sampling to the first 24 hours, lack of long-term neurological outcome assessment, and the absence of ROC analysis to establish clinically useful diagnostic cut-off values. Therefore, larger multicenter prospective studies with standardized protocols, serial biomarker assessment, and long-term follow-up are required before these biomarkers can be incorporated into routine pediatric neurocritical care.

Despite the encouraging findings of the present study, further research is required before serum NSE and S100B can be incorporated into routine clinical practice. Future multicenter studies including diverse etiologies of pediatric status epilepticus should validate the diagnostic and prognostic performance of these biomarkers and determine whether their utility varies according to seizure etiology. Integration of serum biomarkers with quantitative

electroencephalography, neuroimaging, and clinical severity scores may further improve early risk stratification Before routine clinical implementation, standardized sampling protocols, assay methods, reference ranges, and validated diagnostic cut-off values must be established. Because both NSE and S100B may be elevated in a variety of neurological and systemic disorders, they should be regarded as adjunctive biomarkers that complement, rather than replace, clinical assessment, electroencephalography, and neuroimaging.

In summary, serum NSE and S100B were significantly elevated in children with idiopathic convulsive status epilepticus, increased progressively during the first 24 hours after seizure onset, and correlated with seizure duration and treatment intensity, supporting their potential role as biomarkers of seizure-induced neuronal and astroglial injury. However, the relatively small sample size, single-center design, and absence of long-term outcome assessment limit the clinical applicability of these findings. Accordingly, larger multicenter prospective studies incorporating serial biomarker measurements, ROC analysis, multivariable prediction models, and long-term neurological follow-up are required before routine clinical use can be recommended.

CONCLUSION:

Serum neuron-specific enolase (NSE) and S100 calcium-binding protein B (S100B) concentrations were significantly elevated in children with idiopathic convulsive status epilepticus compared with children with well-controlled idiopathic epilepsy. Both biomarkers increased during the first 24 hours after seizure onset and correlated positively with seizure duration and the number of antiseizure medications required for seizure control, indicating that they reflect the severity of seizure-induced neuronal and astroglial injury.

These findings support the potential role of NSE and S100B as complementary biomarkers of acute brain injury following prolonged convulsive seizures. However, because both biomarkers lack disease specificity, they should be interpreted as adjunctive indicators alongside clinical assessment, electroencephalography, and neuroimaging rather than as diagnostic markers of status epilepticus.

Given the relatively small sample size, single-center design, and absence of long-term outcome assessment, routine clinical use of serum NSE and S100B cannot yet be recommended. Larger multicenter prospective studies are needed to validate their diagnostic and prognostic value and to establish standardized sampling protocols and clinically meaningful cut-off values before routine implementation in pediatric neurocritical care.

REFERENCES:

1. **Migdady, I., Rosenthal, E. S., & Cock, H. R.** Management of status epilepticus: a narrative review. Anaesthesia, 2022, 77, 78-91.
2. **Coppler, P. J., & Elmer, J.** Status epilepticus: a neurologic emergency. Critical Care Clinics, 2023, 39(1), 87-102.
3. **Beniczky, S., Trinka, E., Wirrell, E., Abdulla, F., Al Baradie, R., Alonso Vanegas, M., & Cross, J. H.** Updated classification of epileptic seizures: Position paper of the International League Against Epilepsy. Epilepsia, 2025, 66(6), 1804-1823.
4. **Ascoli, M., Ferlazzo, E., Gasparini, S., Mastroianni, G., Citraro, R., Roberti, R., & Russo, E.** Epidemiology and outcomes of status epilepticus. International Journal of General Medicine, 2021, 2965-2973.
5. **Leitinger, M., Bosque-Varela, P., Kuchukhidze, G., Leitner, U., Höfler, J., Kalss, G., & Trinka, E.** Seminars in epileptology: How to diagnose status epilepticus in adults and children. Epileptic Disorders, 2025, 27(4), 530-549.
6. **Matricardi, S., Scorrano, G., Prezioso, G., Burchiani, B., Di Cara, G., Striano, P., & Verrotti, A.** The latest advances in the pharmacological management of focal epilepsies in children: a narrative review. Expert Review of Neurotherapeutics, 2024, 24(4), 371-381.
7. **Rho, J. M., & Boison, D.** The metabolic basis of epilepsy. Nature Reviews Neurology, 2022, 18(6), 333-347.
8. **Meletti, S., Hanin, A., Giovannini, G., Bedin, R., Burani, M., Taruffi, L., & Hirsch, L. J.** Acute Brain Injury in New-Onset Refractory Status Epilepticus and Etiology-Defined Status Epilepticus. JAMA neurology, 2026, 83(6), 563-572.
9. **Westover, M. B., Gururangan, K., Markert, M. S., Blond, B. N., Lai, S., Benard, S., & Parvizi, J.** Diagnostic value of electroencephalography with ten electrodes in critically ill patients. Neurocritical care, 2020, 33(2), 479-490.
10. **Arslan, B., & Zetterberg, H.** Fluid Markers of Axonal and Neuronal Injury. Biomarkers of Neurodegenerative Disorders: Current Progress and Future Directions, 2025, 109-124.
11. **Patabendige, A., & Janigro, D.** The role of the blood–brain barrier during neurological disease and infection. Biochemical Society Transactions, 2023, 51(2), 613-626.
12. **Garcia-Alix, A., & Arnaez, J.** Value of brain damage biomarkers in cerebrospinal fluid in neonates with hypoxic–ischemic brain injury. Biomarkers in Medicine, 2022, 16(2), 117-125.
13. **Bolon, B., & Kornegay, J. N.** A Fandango of Form and Function: The Interplay between Clinical Neurology and Neuropathology Evaluation. Toxicologic Pathology, 2025, 53(4), 321-344.
14. **Arrais, A. C., Melo, L. H. M., Norrara, B., Almeida, M. A. B., Freire, K. F., Melo, A. M. M., & Cavalcanti, J. R. L.** S100B protein: general characteristics and pathophysiological implications in

the Central Nervous System. International Journal of Neuroscience, 2022, 132(3), 313-321.

15. **Halford, J., Shen, S., Itamura, K., Levine, J., Chong, A. C., Czerwieniec, G., & Wanner, I. B.** New astroglial injury-defined biomarkers for neurotrauma assessment. Journal of Cerebral Blood Flow & Metabolism, 2017, 37(10), 3278-3299.
16. **Zhang, H., Wang, J., Qu, Y., Yang, Y., & Guo, Z. N.** Brain injury biomarkers and applications in neurological diseases. Chinese medical journal, 2025, 138(01), 5-14.
17. **Sokolowski, K., Liu, J., Delatte, M. S., Authier, S., McMaster, O., & Bolon, B.** The role of neuropathology evaluation in the nonclinical assessment of seizure liability. Toxicologic Pathology, 2024, 52(8), 566-573.
18. **Simani, L., Sadeghi, M., Ryan, F., Dehghani, M., & Niknazar, S.** Elevated blood-based brain biomarker levels in patients with epileptic seizures: a systematic review and meta-analysis. ACS Chemical Neuroscience, 2020, 11(24), 4048-4059.
19. **Tan, T. H. L., Perucca, P., O'Brien, T. J., Kwan, P., & Monif, M.** Inflammation, ictogenesis, and epileptogenesis: an exploration through human disease. Epilepsia, 2021, 62(2), 303-324.
20. **Samanta, D., Garrity, L., & Arya, R.** Refractory and super-refractory status epilepticus. Indian pediatrics, 2020, 57(3), 239-253.
21. **Sun, H., Li, X., Guo, Q., & Liu, S.** Research progress on oxidative stress regulating different types of neuronal death caused by epileptic seizures. Neurological Sciences, 2022, 43(11), 6279-6298.
22. **Gayger-Dias, V., Vizuete, A. F., Rodrigues, L., Wartchow, K. M., Bobermin, L., Leite, M. C., & Gonçalves, C. A.** How S100B crosses brain barriers and why it is considered a peripheral marker of brain injury. Experimental Biology and Medicine, 2023, 248(22), 2109-2119.
23. **Hanin, A., Lambrecq, V., Denis, J. A., Imbert-Bismut, F., Rucheton, B., Lamari, F., & Navarro, V.** Cerebrospinal fluid and blood biomarkers of status epilepticus. Epilepsia, 2020, 61(1), 6-18.
24. **Rajagopalan, S., & Sarwal, A.** Neuromonitoring in critically ill patients. Critical Care Medicine, 2023, 51(4), 525-542.
25. **Banote, R. K., Akel, S., & Zelano, J.** Blood biomarkers in epilepsy. Acta Neurologica Scandinavica, 2022, 146(4), 362-368.
26. **Vezzani, A., Balosso, S., & Ravizza, T.** Neuroinflammatory pathways as treatment targets and biomarkers in epilepsy. Nature Reviews Neurology, 2019, 15(8), 459-472.
27. **Cresto, N., Givalois, L., Badaut, J., Janvier, A., Genin, A., Audinat, E., & Marchi, N.** Bursts of brain erosion: seizures and age-dependent neurological vulnerability. Trends in Molecular Medicine, 2025, 31(6), 535-547.
28. **Prakash, A. J., Adan, A., Chauhan, K., Weeraman, P. W. J. K., Mapitigama, K. O. P., & Abusara, O.** Neuroprognostication in the First Six hours. Junior Researchers, 2026, 4(1), 1-18.
29. **Wang, P., Huang, J., Wen, H., Liang, X., Wang, J., Ding, P., & Ding, J.** Clinical significance of GABA, NSE, and miR-155 expression in patients with post-stroke epilepsy. Neuroscience, 2025, 571, 151-158.
30. **Macedo, R. C. D., Tomasi, C. D., Giombelli, V. R., Alves, S. C., Bristot, M. D. L. U., Locks, M. F. T., ... & Ritter, C.** Lack of association of S100β and neuron-specific enolase with mortality in critically ill patients. Revista Brasileira de Psiquiatria, 2013, 35(3), 267-270.
31. **Lybeck, A., Friberg, H., Nielsen, N., Rundgren, M., Ullen, S., Zetterberg, H., & Westhall, E.** Postanoxic electrographic status epilepticus and serum biomarkers of brain injury. Resuscitation, 2021, 158, 253-257.
32. **Perucca, E., Perucca, P., White, H. S., & Wirrell, E. C.** Drug resistance in epilepsy. The Lancet Neurology, 2023, 22(8), 723-734.
33. **Hanin, A., Marois, C., Guillemaud, M., Chavez, M., Cosme, L., Hayatou, Z., & Navarro, V.** Exploring pathways leading to drug-resistant epilepsy for patients with cryptogenic new onset refractory status epilepticus. Epilepsia, 2026, 67(5), 2326-2346.
34. **Langeh, U., & Singh, S.** Targeting S100B protein as a surrogate biomarker and its role in various neurological disorders. Current neuropharmacology, 2021, 19(2), 265-277.
35. **Farhan, R., Hashmi, S. A., Kapur, J., D'Abreu, A., Punia, V., Manning, C., & Zawar, I.** Exploring biomarkers of neurodegeneration in epilepsy: Critical insights. Epileptic Disorders, 2025, 27(3), 341-357.
36. **Gaitsch, H., Franklin, R. J., & Reich, D. S.** Cell-free DNA-based liquid biopsies in neurology. Brain, 2023, 146(5), 1758-1774.