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Original Research Article

Changes of Biochemical Biomarkers in the Serum of Children with Convulsive Status Epilepticus: A Cross-Sectional Study

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Abstract

Background: Convulsive status epilepticus (CSE) is a neurological emergency in children associated with significant morbidity and mortality. Prolonged seizures may result in metabolic derangements, systemic inflammatory response, and neuronal injury. Identification of serum biochemical biomarkers may help assess severity, etiology, and early prognosis.

Objective: To evaluate changes in selected biochemical biomarkers in children presenting with convulsive status epilepticus and to analyse their association with clinical parameters.

Materials and Methods: This hospital-based cross-sectional study included 100 children aged 1 month to 12 years presenting with CSE. Serum lactate, creatine kinase (CK), neuron-specific enolase (NSE), interleukin-6 (IL-6), C-reactive protein (CRP), procalcitonin, cortisol, electrolyte profile (Na^+, K^+, Ca^{2+}), and serum glucose were measured within 6 hours of admission. Statistical analysis included descriptive statistics, independent t-test, ANOVA, and correlation analysis.

Results: Serum lactate, CK, NSE, IL-6, CRP, and cortisol were significantly elevated in children with seizure duration >30 minutes ($p<0.05$). Electrolyte abnormalities were observed in 32% of cases, with hyponatremia being most common. NSE and IL-6 levels positively correlated with seizure duration ($r=0.48$ and $r=0.52$ respectively, $p<0.001$).

Conclusion: Children with convulsive status epilepticus demonstrate significant biochemical alterations reflecting hypoxia, muscle injury, neuroinflammation, and neuronal damage. Early biomarker assessment may aid in risk stratification and management.

Keywords: Convulsive Status Epilepticus, Biomarkers, NSE, IL-6, Lactate, Pediatric Seizures.

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Introduction

Convulsive status epilepticus (CSE) is one of the most serious neurological emergencies in pediatric practice, defined operationally as a continuous seizure lasting ≥5 minutes or recurrent seizures without recovery of consciousness between events, requiring urgent intervention to prevent long-term injury [1]. The incidence of status epilepticus in children ranges widely but remains a significant cause of morbidity and mortality globally, with the highest rates observed in infants and young children [2]. Pediatric etiologies are diverse and include febrile seizures, central nervous system infections, metabolic derangements, structural brain anomalies, and idiopathic epilepsy; in low-resource settings, infectious and metabolic causes are especially prevalent [3].

Prolonged convulsive activity initiates a cascade of pathophysiological events, including excessive neuronal firing, increased cerebral metabolic demand, oxidative stress, excitotoxicity, systemic inflammatory activation, and blood–brain barrier disruption [4]. When metabolic demand outpaces oxygen and glucose delivery, anaerobic metabolism ensues, leading to raised serum lactate levels, which may serve as early markers of seizure severity and tissue hypoxia [5]. Concurrently, sustained muscle activity increases creatine kinase (CK) levels, potentially leading to rhabdomyolysis and secondary complications [6]. Beyond

metabolic stress, prolonged seizures induce neuronal injury and neuroinflammatory responses. Neuron-specific enolase (NSE), released from injured neurons, has been reported to correlate with seizure duration and neurological outcome severity [7].

Inflammatory mediators such as interleukin-6 (IL-6) increase during and after prolonged seizures, reflecting activation of systemic and central inflammatory pathways [8]. Additional biomarkers like C-reactive protein (CRP) and procalcitonin may rise in response to infection or systemic inflammation, aiding differentiation of infectious versus non-infectious seizure triggers [9]. Stress responses mediated by the hypothalamic–pituitary–adrenal axis can elevate cortisol levels during acute CSE, providing insight into physiological stress burden and potentially correlating with severity [10]. Electrolyte disturbances—particularly hyponatremia, hypoglycemia, and hypocalcemia—are both precipitants and consequences of prolonged seizures and require early identification to guide management [11].

Given the interplay of hypoxia, metabolic stress, inflammation, and neuronal injury in pediatric CSE, evaluating serum biochemical biomarkers may offer objective insights into disease severity, etiology, and prognosis. However, pediatric-specific data—especially from developing regions—remain limited, highlighting the need for systematic biomarker evaluation in children with CSE. The study aims to assess changes in serum biomarkers—including lactate, CK, NSE, IL-6, CRP, procalcitonin, cortisol, electrolytes, and glucose—in children with convulsive status epilepticus and correlate them with seizure duration, etiology, and severity for potential prognostic use.

Materials and Methods

Study Design: Hospital-based cross-sectional study.

Study Setting: Department of Paediatrics, tertiary care hospital.

Study Duration: 12 months.

Sample Size: 100 children diagnosed with convulsive status epilepticus.

Inclusion Criteria

- Age 1 month to 12 years
- Convulsive seizures lasting ≥5 minutes
- Admission within 6 hours of seizure onset

Exclusion Criteria

- Known neuromuscular disorders
- Chronic liver or renal disease
- Recent trauma

Data Collection

Clinical data recorded:

- Age
- Sex
- Seizure duration
- Etiology (febrile, structural, metabolic, infectious)

Laboratory Investigations (within 6 hours)

- Serum Lactate
- Serum CK
- NSE
- IL-6
- CRP
- Procalcitonin
- Serum Cortisol
- Sodium, Potassium, Calcium
- Serum Glucose

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while Data were entered into Excel and analyzed using SPSS and GraphPad Prism. Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data. Chi-square tests (including Fisher's exact test for small sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Results

Table 1: Demographic Characteristics (n=100)

Variable	Frequency	Percentage
Age <5 years	62	62%
Age 5–12 years	38	38%
Male	58	58%
Female	42	42%

Table 2: Mean Biomarker Levels

Parameter	Mean ± SD	Reference Range
Serum Lactate (mmol/L)	4.8 ± 1.6	0.5–2.2
CK (U/L)	420 ± 180	20–200
NSE (ng/mL)	32 ± 11	<16
IL-6 (pg/mL)	48 ± 22	<7
CRP (mg/L)	18 ± 10	<5
Procalcitonin (ng/mL)	1.9 ± 1.2	<0.5
Cortisol (µg/dL)	28 ± 9	5–25
Sodium (mEq/L)	133 ± 4	135–145
Potassium (mEq/L)	4.7 ± 0.8	3.5–5.5
Calcium (mg/dL)	8.3 ± 0.7	8.5–10.5
Glucose (mg/dL)	128 ± 35	70–110

Table 3: Biomarker Levels According to Seizure Duration

Biomarker	<30 min (n=55)	≥30 min (n=45)	p-value
Lactate	3.9 ± 1.2	5.9 ± 1.4	<0.001
CK	350 ± 120	510 ± 160	<0.001
NSE	25 ± 8	41 ± 10	<0.001
IL-6	32 ± 15	67 ± 18	<0.001
CRP	12 ± 7	25 ± 9	<0.01

Table 4: Electrolyte Abnormalities

Abnormality	Frequency	Percentage
Hyponatremia	22	22%
Hypernatremia	4	4%
Hypocalcemia	10	10%
Hyperkalemia	6	6%

Table 5: Correlation with Seizure Duration

Parameter	Correlation Coefficient (r)	p-value
Lactate	0.44	<0.001
NSE	0.48	<0.001
IL-6	0.52	<0.001
CK	0.39	0.002

Table 6: Etiology Distribution

Etiology	Frequency	Percentage
Febrile	36	36%
CNS Infection	28	28%
Structural	18	18%
Metabolic	12	12%
Unknown	6	6%

A total of 100 children presenting with convulsive status epilepticus were enrolled in the study during the study period. All patients fulfilled the inclusion criteria and had serum biomarker assessment performed within 6 hours of admission.

The majority of children were below 5 years of age (62%), while 38% were between 5 and 12 years. The mean age of the study population was 4.6 ± 3.1 years. There was a slight male predominance, with 58 males (58%) and 42 females (42%), yielding a male-to-female ratio of 1.38:1. Febrile seizures were the most common etiology (36%), followed by central nervous system infections (28%), structural causes (18%), metabolic causes (12%), and unknown etiology (6%). Children with CNS infections and structural etiologies were more likely to have prolonged seizure duration (≥30 minutes). Fifty-five children (55%) had seizure duration less than 30 minutes, while 45 children (45%) had seizures lasting 30 minutes or more. The mean seizure duration was 28.4 ± 12.6 minutes. Significant alterations were observed in multiple biochemical parameters. The mean serum lactate level was 4.8 ± 1.6 mmol/L, which was elevated above the normal reference range in 68% of children.

Children with seizure duration ≥30 minutes had significantly higher lactate levels (5.9 ± 1.4

mmol/L) compared to those with shorter duration seizures (3.9 ± 1.2 mmol/L), and this difference was statistically significant (p<0.001).Mean CK level was 420 ± 180 U/L. Elevated CK levels were observed in 61% of children. Patients with prolonged seizures showed significantly higher CK levels (510 ± 160 U/L) compared to those with shorter seizures (350 ± 120 U/L) (p<0.001). The mean NSE level was 32 ± 11 ng/mL, with 72% of children demonstrating elevated values above the normal reference range. NSE levels were significantly higher in children with seizure duration ≥30 minutes (41 ± 10 ng/mL) compared to those with shorter seizures (25 ± 8 ng/mL) (p<0.001). Mean IL-6 level was 48 ± 22 pg/mL. Elevated IL-6 levels were noted in 70% of cases. Children with prolonged seizures exhibited markedly higher IL-6 levels (67 ± 18 pg/mL) compared to those with seizures <30 minutes (32 ± 15 pg/mL), showing strong statistical significance (p<0.001). The mean CRP level was 18 ± 10 mg/L. Elevated CRP was seen in 64% of children, particularly in those with infectious etiologies. Children with CNS infections had significantly higher CRP levels (26 ± 8 mg/L) compared to non-infectious causes (12 ± 6 mg/L) (p<0.01). The mean procalcitonin level was 1.9 ± 1.2 ng/mL. Elevated procalcitonin was observed predominantly in children with CNS infections. A statistically significant difference was noted between infectious and non-infectious etiologies (p<0.01). Mean serum cortisol level was 28 ± 9 µg/dL. Elevated cortisol levels were observed in 58% of cases, reflecting physiological stress response. Children with seizure duration ≥30 minutes had significantly higher cortisol levels (32 ± 8 µg/dL) compared to those with shorter seizures (24 ± 7 µg/dL) (p=0.003). Electrolyte abnormalities were identified in 32% of children with convulsive status epilepticus, with hyponatremia being the most common disturbance (22%), followed by hypocalcemia (10%), hyperkalemia (6%), and hypernatremia (4%). Notably, children with hyponatremia demonstrated a significantly higher likelihood of experiencing recurrent seizures during hospitalization (p = 0.04), suggesting a potential association between sodium imbalance and seizure recurrence. The mean serum glucose level was 128 ± 35 mg/dL. Hyperglycemia (>140 mg/dL) was observed in 34% of children, particularly in those with prolonged seizures. Hypoglycemia was observed in 6% of cases. Pearson correlation analysis demonstrated significant positive associations between seizure duration and several biochemical biomarkers. A moderate positive correlation was observed with serum lactate (r = 0.44, p < 0.001) and neuron-specific enolase (NSE) (r = 0.48, p < 0.001), while interleukin-6 (IL-6) showed a strong positive correlation (r = 0.52, p < 0.001). Creatine kinase (CK) also exhibited a positive correlation with seizure duration (r = 0.39, p = 0.002), and cortisol demonstrated a mild but statistically significant positive correlation (r = 0.31, p = 0.01). In contrast, potassium levels did not show a statistically significant correlation with seizure duration. Children with CNS infections had significantly higher inflammatory markers (IL-6, CRP, procalcitonin) compared to febrile and structural etiologies (p<0.01). However, NSE elevation was observed across all etiological categories, suggesting neuronal injury irrespective of underlying cause. Lactate elevation was most pronounced in prolonged generalized tonic-clonic seizures irrespective of etiology.

Discussion

The demographic profile of our study population, with a predominance of children below 5 years (62%) and a slight male preponderance (58%), is consistent with established epidemiological data indicating higher incidence of status epilepticus in younger age groups, as reported by Gurcharran K et al [13 (2019)] and Ngugi AK et al [15 (2010)]. The predominance of febrile seizures (36%) followed by CNS infections (28%) aligns with observations in pediatric cohorts from developing regions, where infectious etiologies significantly contribute to seizure burden, as described by Behera K et al [4 (2005)] and Gurcharran K et al [13 (2019)].

The finding that 45% of children experienced seizures lasting ≥30 minutes highlights the substantial proportion at risk of neuronal injury, in accordance with the operational definition and time-dependent pathophysiological changes described by Trinka E et al [1 (2015)]. Prolonged seizure activity has been associated with metabolic stress, excitotoxicity, and systemic complications, reinforcing the importance of early biochemical assessment.

Elevated serum lactate in 68% of children, with significantly higher levels in prolonged seizures (p<0.001), supports the concept of seizure-induced tissue hypoxia and anaerobic metabolism. Similar findings were reported by Wang M et al [12 (2022)], who demonstrated significantly raised lactate levels in pediatric convulsive status epilepticus, correlating positively with seizure duration (p<0.001). Elevated CK levels in 61% of our cohort, particularly in prolonged seizures, reflect sustained muscle activity and risk of rhabdomyolysis, consistent with metabolic stress responses described in pediatric status epilepticus [2 (2014)]. The marked elevation of NSE in 72% of children and its strong association with prolonged seizures supports its role as a marker of neuronal injury. DeGiorgio CM [6 (1994)] reported significant NSE elevation following status epilepticus, correlating with seizure severity.

Similarly, Wang M et al [12 (2022)] observed NSE elevation in approximately 70% of pediatric cases, with significant correlation to seizure duration ($r \approx 0.45$). Inflammatory activation was evident through elevated IL-6 (70%) and CRP (64%), particularly among children with CNS infections. Alapirtti T et al [7 (2009)] demonstrated increased IL-6 production during seizure activity, while Madžar D et al [19 (2021)] showed that higher CRP levels were associated with worse outcomes in status epilepticus ($p<0.05$). The higher procalcitonin levels in infectious etiologies further support its utility in differentiating bacterial causes. Electrolyte abnormalities (32%), especially hyponatremia (22%), and its association with recurrent seizures ($p=0.04$) highlight the bidirectional relationship between electrolyte imbalance and seizure activity. The hyperglycemia observed in 34% of children and elevated cortisol levels (58%) reflect stress-mediated neuroendocrine activation, consistent with systemic stress responses in prolonged seizures [2 (2014)]. Overall, the positive correlations between seizure duration and lactate, NSE, IL-6, CK, and cortisol reinforce the time-dependent biochemical cascade underlying neuronal injury and systemic inflammation. These findings support the growing evidence that serum biomarkers may serve as adjunctive tools for severity assessment and early prognostication in pediatric convulsive status epilepticus.

Conclusion

This study demonstrates that children presenting with convulsive status epilepticus exhibit significant alterations in biochemical biomarkers reflecting systemic metabolic stress, neuroinflammation, and neuronal injury. Serum lactate and creatine kinase indicate hypoxic and muscular consequences of prolonged convulsions, while elevated neuron-specific enolase suggests neuronal damage. Interleukin-6 showed the strongest correlation with seizure duration, underscoring the pivotal role of inflammatory pathways in seizure pathophysiology. Electrolyte disturbances, particularly hyponatremia, were common and warrant prompt correction. Early assessment of selected serum biomarkers may provide valuable adjunctive information regarding seizure severity and underlying etiology.

Incorporation of these biochemical parameters into clinical evaluation protocols could improve risk stratification and guide timely therapeutic interventions. Further longitudinal studies are required to determine the prognostic utility of these biomarkers in predicting long-term neurological outcomes in children with convulsive status epilepticus.

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