DOI: 10.7860/JCDR/2026/88125.24683

Original Article

Paediatrics Section

Cerebrospinal Fluid Levels of Brain Derived Neurotrophic Factor in Children with Acute Encephalitis Syndrome: A Prospective Observational Study

SHIV KANT PRAKRATYANSH[1], CHANDRAKANTA[2], MANISHA VERMA[3], NEERAJ ANAND[4], SHAILENDRA K SAXENA[5]

BY-NC-ND

ABSTRACT

Introduction: Acute Encephalitis Syndrome (AES) is a severe neurological condition affecting children, characterised by acute onset of fever, altered consciousness, and seizures, often leading to long-term complications or death. Brain Derived Neurotrophic Factor (BDNF) is a neurotrophin involved in neuronal survival, development, and repair, as well as in the brain's response to injury and inflammation. Although BDNF has been studied in other neurological conditions, its role in AES remains largely unexplored.

Aim: To assess BDNF in the Cerebrospinal Fluid (CSF) of children diagnosed with AES to explore its potential role in disease pathophysiology.

Materials and Methods: This prospective observational study was conducted at the Department of Paediatrics at King George's Medical University, Lucknow, Uttar Pradesh, India, from October 2022 to April 2024. Children aged six months to ≤12 years diagnosed with AES as per World Health Organisation (WHO) criteria were enrolled in the study. A detailed history, demographic data and examination, including blood investigations and neuroimaging {Computed Tomography (CT) scan or Magnetic Resonance Imaging (MRI) Brain} were performed as needed for patients. CSF BDNF levels were measured using Enzyme Linked Immunosorbent Assay (ELISA). Outcomes were categorised as good or bad based on clinical status at discharge. Data were entered into a Microsoft Excel spreadsheet and were analysed using the statistical software Statistical Package for the Social Sciences (SPSS) version 23.0. For the comparative data, t-test and Chi-square test were applied. The difference in p-value<0.05 was considered statistically significant.

Results: The present study evaluated 80 paediatric cases of AES with a mean age of 7.95±3.59 years, of which 48 cases (60%) had an unknown aetiology, 25 cases (31.25%) had bacterial infections, and 7 cases (8.75%) had viral infections. No significant differences were found in clinical symptoms, laboratory investigations, or CSF BDNF levels across the groups. Although most children had favourable outcomes (71.25%), there were minor differences in neurological signs, such as absent deep tendon reflexes in bacterial cases. The duration of hospital stay and recovery, as reflected by GCS scores, was similar across all groups.

Conclusion: The present study found no significant difference in BDNF levels across different AES aetiologies or clinical outcomes. However, BDNF's potential as a neuroprotective agent in AES remains promising, warranting further research to explore its therapeutic applications.

Keywords: Biomarkers, Central nervous system infections, Neuroprotection, Neurological outcome, Neuroinflammation

INTRODUCTION

The AES is a major public health concern, especially in children, due to its high rates of morbidity, mortality, and potential for long-term neurological damage [1]. AES is characterised by sudden onset of fever, altered mental status, and seizures, and is often caused by a wide variety of infectious and non infectious agents [2]. The WHO introduced the term AES in 2008 to improve surveillance and case definition, particularly in endemic regions like India [3]. AES prevalence varies, with an annual average of 3.5 to 7.4 cases per 100,000 persons, and it is more prevalent in children [4]. Although viruses are frequently to blame, determining the particular cause is difficult owing to diagnostic challenges and comparable Central Nervous System (CNS) disorders. Between 2008 and 2014, India had about 44,000 AES cases and over 6,000 fatalities, primarily in Uttar Pradesh and Bihar [5]. In 2016, an epidemic in Gorakhpur claimed the lives of nearly 125 children in a single hospital [6].

In India, the aetiology of AES is diverse and often remains unidentified. While Japanese Encephalitis (JE) has historically been the most recognised cause, recent studies have highlighted other agents such as herpes simplex virus, scrub typhus, dengue, and various rickettsial infections [7,8]. Despite extensive diagnostic efforts, a significant proportion of AES cases still have no clear aetiology. This diagnostic uncertainty and the unpredictable clinical course of AES pose challenges in management and prognosis.

The BDNF is a key member of the neurotrophin family involved in the development, maintenance, and plasticity of the nervous system [9]. It plays a critical role in neurogenesis, neuronal survival, and synaptic regulation [9]. BDNF is primarily produced in neuronal and glial cells and is known to be upregulated in response to brain injury or inflammation [9]. Despite its well-studied role in mammalian brain development and synaptic transmission [10], the function of BDNF in AES remains unclear. CSF serves as a vital indicator of CNS function, capable of revealing metabolic changes in the brain and spinal cord.

Measuring BDNF levels in the CSF of AES patients may provide insight into disease mechanisms and help identify potential prognostic markers. Although BDNF has been studied in other neurological conditions [11], there is a scarcity of data on its role in AES, especially in paediatric populations from developing countries.

Given this gap in knowledge, the present study aimed to evaluate the levels of BDNF in the CSF of children diagnosed with AES, with the goal of better understanding its potential role in disease pathogenesis and severity.

MATERIALS AND METHODS

This prospective observational study was conducted at the Department of Paediatrics at King George's Medical University, Lucknow, a tertiary care teaching hospital in Uttar Pradesh, India, over a period of 18 months, from October 2022 to April 2024. The study was approved by the Institutional Ethics Committee (Reference code: XIV-PGTSC-IIA/P27). Written informed consent was obtained from parents/guardians. Due to the altered sensorium in most patients, assent could not be obtained.

Inclusion criteria: Children of either gender, aged between 6 months and ≤12 years, admitted with AES as defined by the WHO [3], were enrolled. Inclusion criteria consisted of children presenting with an acute onset (≤7 days) of fever with altered mental status lasting more than 12 hours, with and without seizures.

Exclusion criteria: Children were excluded if informed consent was not obtained, if they presented with febrile seizures, or if they had a known non infectious aetiology for CNS symptoms, such as trauma, toxic exposure, stroke, malignancy, epilepsy, metabolic disorders, or poisoning. Additionally, children with pre-existing neurological disorders were also excluded from the study.

Study Procedure

A total of 80 AES cases who presented within the study period were included. Detailed history, clinical presentation, physical examination, and laboratory findings were recorded using a structured proforma. Investigations included:

- Complete Blood Count (CBC), liver and renal function tests, and serum electrolytes.
- Neuroimaging (CT/MRI) as indicated.
- Lumbar puncture for CSF analysis.
- Etiological work-up: JE IgM (CSF), HSV PCR (CSF), Dengue IgM (serum), Scrub Typhus IgM (blood), Leptospira IgM (blood), pyogenic culture (CSF), TB CBNAAT (CSF and gastric aspirate).

Measurement of BDNF levels: The CSF samples of 0.5 mL for each measurement were centrifuged at 5000 rpm for 10 minutes, and supernatants were stored at -70°C until analysis. BDNF levels were measured using a human BDNF ELISA kit (FineTest, Wuhan, China; Catalog No. EH0043, 96T, Batch No. FN231117) at the Centre for Advanced Research (CFAR), King George's Medical University (KGMU).

Outcome Assessment: Children were followed until discharge. Outcomes were assessed based on the Glasgow Coma Scale (GCS), duration of hospital stay, presence of seizures, focal neurological deficits, abnormal movements, and mode of feeding at discharge.

Outcomes were classified as good outcome (patients discharged in stable condition) and bad outcome {patients who expired, Left Against Medical Advice (LAMA), absconded in poor general condition, or had unstable vitals}.

STATISTICAL ANALYSIS

Data were entered into Microsoft Excel and analysed using SPSS version 23.0. Univariate analysis was performed. For the descriptive data, mean, standard deviation, and percentage were calculated. For the comparative data, t-test and chi-square test were applied. A p-value <0.05 was considered statistically significant.

RESULTS

The present study evaluated a total of 80 paediatric cases of AES. In the present study, the mean age of the participants was 7.95±3.59 years, with the majority (55%) aged between 5-12 years, and predominantly females, 47 (58.75%). Overall, 57 (71.25%) had favourable outcomes. In the present study, the mean CSF BDNF levels were 23.73±5.75 pg/mL [Table/Fig-1].

Demographics and vaccination status		n (%)
Age group (years)	6 months to 1	3 (3.75%)
	1 to 5	33 (41.25%)
	5 to 12	44 (55%)
	Mean±SD	7.95±3.59
Gender	Male	33 (41.25%)
	Female	47 (58.75%)
Vaccination	Not vaccinated	5 (6.25%)
	Fully vaccinated	64 (80%)
	Partially vaccinated	10 (12.5%)
	Not known	1 (1.25%)
Clinical parameters		
Fever		80 (100%)
Fever duration (days) (mean±SD)		6.95±3.82
Headache		18 (22.5%)
Vomiting		28 (35%)
Seizure		78 (97.5%)
Altered sensorium		76 (95%)
Hospital admission in past		0
GCS		8.64±2.38
Tachycardia		44 (55%)
Tachypnoea		39 (48.75%)
Hypotension		4 (5%)
Features of shock		10 (12.5%)
Rash		1 (1.25%)
Bleeding manifestations		3 (3.75%)
Enlarged liver		27 (33.75%)
Enlarged spleen		8 (10%)
Generalised oedema		2 (2.5%)
Altered consciousness		76 (95%)
Meningeal sign		10 (12.5%)
Hypertonia		33 (41.25%)
Brisk reflexes		46 (57.5%)
Bilateral extensor plantar		52 (65%)
Ankle clonus		1 (1.25%)
Papilloedema		8 (10%)
Cranial nerve palsy		0 (0%)
Focal deficit		2 (2.5%)
Outcome		
Good		57 (71.25%)
Bad		23 (28.75%)
CSF BDNF level		
BDNF levels (pg/mL) (Mean±SD)		23.73±5.75

[Table/Fig-1]: Demographic and clinical variables and CSF BDNF level among children with Acute Encephalitis Syndrome (n=80).

The majority 48 (60%) of the cases had an unknown aetiology, followed by bacterial infections. This distribution highlights that a significant proportion of AES cases remain undiagnosed despite extensive testing [Table/Fig-2].

The comparison of mean BDNF concentrations in CSF across various groups showed no statistically significant differences. Additionally, children with good outcomes (24.45±6.28 pg/mL) had slightly higher BDNF levels compared to those with bad outcomes (22.17±4.12 pg/mL), but the difference was not statistically

significant (p=0.112). These findings suggest that CSF BDNF levels do not significantly vary with different aetiologies or outcomes in AES [Table/Fig-3].

Aetiology group	Specific aetiology	n (%)
Viral group	Japanese Encephalitis (JE)	4 (5.00)
	Dengue	3 (3.75)
	Herpes Simplex Virus (HSV)	0 (0.00)
Total viral		7 (8.75)
Bacterial group	Scrub Typhus	20 (25.00)
	Leptospira	5 (6.25)
Total bacterial		25 (31.25)
Unknown group (Undiagnosed)	-	48 (60.00)
Total	-	80

[Table/Fig-2]: Distribution of AES patients according to presence of different aetiology.

Group comparison	n	Mean±SD (pg/mL)	p-value
Aetiological groups			
Viral	7	23.23±8.34	0.354
Bacterial	25	22.50±3.18	
Unknown	48	24.54±6.42	
Viral subtypes			
Japanese Encephalitis (JE)	4	23.44±9.88	0.949
Dengue	3	22.97±7.88	
Bacterial subtypes			
Scrub typhus	20	23.22±3.35	0.637
Leptospira	5	23.22±2.91	
Outcome-based comparison			
Good outcome	57	24.45±6.28	0.112
Bad outcome	23	22.17±4.12	

[Table/Fig-3]: Comparison of mean BDNF concentrations in CSF across different groups.

The demographic comparison among viral, bacterial, and unknown AES groups showed no statistically significant differences in age, gender, socioeconomic status, or vaccination status (p-values are 0.167, 0.722, 0.898, and 0.688, respectively).

On comparing outcomes across different aetiologies of AES, good outcomes were observed in 71.43% (5 out of 7) of viral cases, 80% (20 out of 25) of bacterial cases, and 66.67% (32 out of 48) of unknown cases. Among bacterial subtypes, Scrub typhus had a higher good outcome rate (85%) compared to Leptospira (66.67%). However, these differences were not statistically significant (p>0.05), indicating similar outcome distributions across all groups [Table/Fig-4].

The results indicate that there were no significant differences in most clinical parameters between the viral, bacterial, and unknown groups. Blood investigations did not show any significant differences between the groups except serum bilirubin values [Table/Fig-5].

Overall, the groups displayed similar clinical characteristics on examination, with only a few differences in neurological signs [Table/Fig-6].

At admission, the severity of neurological impairment, as reflected by the GCS, was similar across the groups, with mean scores of 9.14±3.53 for the viral group, 8.52±2.08 for the bacterial group, and 8.54±2.34 for the unknown group. These differences were not statistically significant (p=0.812), suggesting that the initial severity of acute encephalitis was comparable among all groups. At discharge, all groups showed significant improvement in their GCS scores, with the viral group achieving a perfect score of 15±0.00, and the bacterial and unknown groups showing scores of 14.80±0.62 and 14.48±1.72, respectively. However, the differences in GCS at discharge were also not statistically significant (p=0.592), indicating that recovery was similar across the groups.

Demographic status	Viral (n=7) n (%)	Bacterial (n=25) n (%)	Unknown (n=48) n (%)	p-Value
Age (in years)				
6 months to 1	0	1 (4.00%)	2 (4.17%)	0.167
1-5	0	10 (40.00%)	23 (47.92%)	
5-12	7 (100.00%)	14 (56.00%)	23 (47.92%)	
Gender				
Male	3 (42.86%)	9 (36.00%)	22 (45.83%)	0.722
Female	4 (57.14%)	16 (64.00%)	26 (54.17%)	
Socioeconomic Status (SES)				
Lower	7 (100.00%)	21 (84.00%)	37 (77.08%)	0.898
Middle	0	4 (16.00%)	11 (22.92%)	
Vaccination status				
No vaccinated	1 (14.29%)	1 (4.00%)	3 (6.25%)	0.688
Partially vaccinated	0	2 (8.00%)	8 (16.66%)	
Fully vaccinated	6 (85.71%)	22 (88.00%)	36 (75.00%)	
Not known	0	0	1 (2.08%)	
Outcome				
Good outcome	5 (71.43%)	20 (80%)	32 (66.67%)	0.490
Bad outcome	2 (28.57%)	5 (20%)	16 (33.33%)	

[Table/Fig-4]: Detailed comparison of the demographic characteristics and outcomes of children with AES across viral, bacterial, and unknown groups.

Parameters	Viral (n=7)	Bacterial (n=25)	Unknown (n=48)	p-value
Clinical parameters				
Fever	7 (100.00%)	25 (100.00%)	48 (100.00%)	-
Headache	3 (42.86%)	6 (24.00%)	10 (20.83%)	0.712
Vomiting	4 (57.14%)	12 (48.00%)	13 (27.08%)	0.102
Seizures	7 (100.00%)	24 (96.00%)	47 (97.92%)	0.801
Altered sensorium	7 (100.00%)	24 (96.00%)	45 (93.75%)	0.749
Past history of previous admission	0	0	0	-
Wasting	1 (14.29%)	3 (12.00%)	10 (20.83%)	0.307
Stunting	0	0	2 (4.17%)	-
Duration of fever (Days)	6.14±4.41	7.52±3.99	6.71±3.75	0.603
Duration of seizures (Days)	3.29±2.06	3.16±2.62	2.75±2.03	0.687
Number of seizure episodes/day	2.43±0.79	2.12±0.88	2.31±1.11	0.677
Blood investigation results				
Hb (g/dL)	10.79±2.42	9.75±1.54	10.00±1.88	0.422
TLC (×10³/µL)	11.89±4.13	13.03±7.63	12.76±7.20	0.933
DLC N (%)	74.71±5.50	63.40±13.54	68.06±11.02	0.058
DLC L (%)	21.71±5.65	31.60±13.16	27.67±11.02	0.110
Platelet (x10³/µL)	1.63±1.26	1.57±0.93	1.99±1.19	0.291
S Urea (mg/dL)	59.00±27.05	40.22±23.77	40.33±19.07	0.092
S Creatinine (mg/dL)	0.73±0.25	0.62±0.18	0.60±0.24	0.351
S Bil Total (mg/dL)	0.82±0.37	0.48±0.28	0.51±0.32	0.039
S Bil Direct (mg/dL)	0.51±0.29	0.31±0.18	0.26±0.15	0.003
SGOT (U/L)	106.00±70.56	189.56±230.79	158.40±180.64	0.573
SGPT (U/L)	86.71±95.06	123.50±272.44	84.74±98.09	0.652
Total Protein (g/dL)	6.31±1.08	5.47±0.80	5.85±1.07	0.106
S Albumin (g/dL)	3.38±0.74	3.21±0.67	3.56±0.64	0.101
Potassium (mEq/L)	3.98±0.75	4.34±0.52	4.00±0.59	0.065
Calcium (mg/dL)	4.10±0.35	4.21±0.58	4.03±0.47	0.333
Sodium (mEq/L)	136.14±8.59	135.52±6.14	134.81±6.20	0.823
Cell Count (x10³/µL)	12.71±5.62	11.32±5.83	14.71±12.64	0.422

Polymorphs (%)	12.14±3.93	14.68±5.33	15.10±6.11	0.446
Protein (mg/dL)	124.34±57.51	99.60±43.07	105.12±55.71	0.544
Sugar (mg/dL)	72.17±27.10	62.58±12.54	63.98±25.00	0.594

[Table/Fig-5]: Clinical parameters and blood investigation results across the viral, bacterial, and unknown groups.

Vital parameters/ examination findings	Viral (n=7)	Bacterial (n=25)	Unknown (n=48)	p-value
Lymphadenopathy	0	0	0	-
Shock at time of admission	1 (14.29%)	4 (16.00%)	5 (10.42%)	-
Any meningeal signs	1 (14.29%)	4 (16.00%)	5 (10.42%)	-
Fundus	7 (100.00%)	21 (84.00%)	44 (91.67%)	0.382
Cranial nerve palsy	0	0	0	-
Heart rate				
Normal	4 (57.14%)	10 (40.00%)	22 (45.83%)	0.852
Tachycardia	3 (42.86%)	15 (60.00%)	26 (54.17%)	
Bradycardia	0	0	1 (2.08%)	
Respiratory rate				
Normal	4 (57.14%)	9 (36.00%)	27 (56.25%)	0.302
Increased	3 (42.86%)	16 (64.00%)	19 (39.58%)	
Decreased	0 (0.00%)	0 (0.00%)	2 (4.17%)	
Blood pressure				
Normal	5 (71.43%)	24 (96.00%)	45 (93.75%)	0.181
Hypertension	1 (14.29%)	0 (0.00%)	1 (2.08%)	
Hypotension	1 (14.29%)	1 (4.00%)	2 (4.17%)	
Tone				
Normal	3 (42.86%)	12 (48.00%)	20 (41.67%)	0.752
Exaggerated	2 (28.57%)	9 (36.00%)	22 (45.83%)	
Absent	2 (28.57%)	4 (16.00%)	6 (12.50%)	
Deep tendon reflexes				
Normal	3 (42.86%)	2 (8.00%)	1 (2.08%)	0.001
Exaggerated	4 (57.14%)	10 (40.00%)	14 (29.17%)	
Absent	0	12 (48.00%)	32 (66.67%)	
Planter reflex				
Flexor	3 (42.86%)	6 (24.00%)	13 (27.08%)	0.510
Unilateral extensor	0	0	2 (4.17%)	
Bilateral extensor	3 (42.86%)	18 (72.00%)	32 (66.67%)	
Not elicitable	1 (14.29%)	1 (4.00%)	1 (2.08%)	
Ankle clonus				
Absent	7 (100.00%)	24 (96.00%)	47 (97.92%)	0.801
Present	0	1 (4.00%)	1 (2.08%)	
Focal deficit	0	0	2 (4.17%)	0.505
Rigidity	1 (14.29%)	0	1 (2.08%)	0.097
Posturing	0	0	5 (10.42%)	0.356
Raised intracranial tension	0	0	4 (8.33%)	0.286
Rash	0	1 (4.00%)	0	0.328
Breathing pattern	7 (100.00%)	23 (92.00%)	41 (85.42%)	0.430
Bleeding manifestation	0	1 (4.00%)	2 (4.17%)	0.861
Enlarged liver	4 (57.14%)	10 (40.00%)	12 (25.00%)	0.149
Enlarged spleen	2 (28.57%)	3 (12.00%)	3 (6.25%)	0.170
Oedema	0	0	2 (4.17%)	0.505

[Table/Fig-6]: Comparisons between the viral, bacterial, and unknown groups for various vital parameters and examination findings.

In terms of hospital stay, the bacterial group had the longest duration (118.80±86.52 hours), followed by the unknown group (103.12±66.18 hours), and the viral group had the shortest stay (100±61.91 hours). Despite these differences, the duration of stay did not show a significant variation between the groups (p=0.656), implying that the length of hospitalisation was not influenced by the cause of the encephalitis [Table/Fig-7]. Overall, these findings suggest that while there were some differences in clinical outcomes, particularly in the viral group's rapid recovery, the overall recovery and hospital stay length were comparable across the viral, bacterial, and unknown groups.

Parameters	Viral (n=7) (Mean±SD)	Bacterial (n=25) (Mean±SD)	Unknown (n=48) (Mean±SD)	p-value
GCS at admission	9.14±3.53	8.52±2.08	8.54±2.34	0.812
GCS at discharge	15.00±0.00	14.80±0.62	14.48±1.72	0.592
Duration of hospital stay in hours	100.00±61.91	118.80±86.52	103.13±66.18	0.656

[Table/Fig-7]: GCS at admission/discharge and duration of hospital stay among groups.

No statistically significant differences were observed between different parameters like abnormal movements, focal weakness, seizures and mode of feeding among the groups at discharge [Table/Fig-8].

Groups	Viral (n=5)	Bacterial (n=21)	Unknown (n=33)	p-value
Abnormal movements				
Absent	5 (100%)	20 (95.23%)	33 (100%)	0.398
Present	0	1 (4.77%)	0	
Focal weakness				
Absent	5 (100%)	21 (100%)	32 (96.96%)	0.670
Present	0	0	1 (3.04%)	
Seizures				
Absent	4 (80%)	16 (76.20%)	29 (87.87%)	0.527
Present	1 (20%)	5 (23.8%)	4 (12.13%)	
Mode of feeding				
Oral	5 (100%)	21 (100%)	30 (90.90%)	0.388
Ryle's tube feeding	0	0	3 (9.1%)	

[Table/Fig-8]: Comparison of conditions at discharge between the bacterial, viral, and unknown groups.
Footnote: Abnormal movement includes involuntary movements such as dystonia, chorea, myoclonus, and tremors. Focal weakness includes motor weakness that involves either one limb or half of the body (monoparesis or hemiparesis)

DISCUSSION

The correlation between BDNF and AES holds therapeutic significance. BDNF is renowned for its capacity to enhance neuronal viability, synaptic adaptability, and neurogenesis, rendering it a compelling focus for therapeutic approaches aimed at mitigating the neurological repercussions of AES [12,13].

In the present study, AES was found to be the most prevalent among children aged 5-12 years (55.0%) and was more prevalent in females (58.75%). Moreover, a majority of the children (80.0%) had received vaccinations. These findings align with existing literature, which consistently reports a higher incidence of AES within this age group. For instance, Reddy MN et al., (2019) observed that 55.0% of AES cases in their Indian cohort occurred in children aged 5-15 years [14]. Similarly, Tripathy SK et al., (2019) found a significant concentration of viral AES cases among children in the 5-15 year age bracket, with a median age of six years in viral AES cases and five years in non viral cases (p=0.02) [15]. Gogoi A et al., (2016) reported a mean age of 5.4±3.3 years for AES onset, ranging from one month to 12 years, and noted a male predominance with a male-to-female ratio of 1.5:1 [16].

In the present study, fever was identified as the most common clinical manifestation, occurring in all cases. Seizures were observed in 97.5% of patients, followed by altered sensorium, vomiting, and headache. Notably, none of the children had a prior history of hospitalisation. These findings are supported by Tripathy SK et

al., (2019), who reported that the majority of AES cases presented with fever, impaired consciousness, increased ICP, seizures, and vomiting [15]. Specifically, the viral AES subgroup demonstrated a significantly higher frequency of increased ICP, GCS scores below 8, rash, motor paralysis, and cranial nerve palsies. Reddy MN et al., (2019) also highlighted fever (100%) and altered sensorium (100%) as consistent features, along with convulsions (40%), headache (45%), neurological impairment (40%), and vomiting (50%) [14]. Similarly, Santoso LA et al., (2020) reported that children with encephalitis commonly exhibited reduced levels of consciousness (96%), fever (90%), seizures (87%), and localised neurological deficits (47%) [17].

In this pilot study, the mean GCS score was 8. Tachycardia and tachypnoea were observed in 55% and 48.75% of children, respectively, while shock and hypotension were noted in 12.5% and 5%. In contrast, Majhi SC et al., (2024) reported GCS scores above eight in 83.3% of cases, indicating less severe neurological impairment in their cohort [18]. Although AES primarily affects the CNS, systemic involvement is not uncommon. Hepatomegaly (33.75%) and splenomegaly (10%) were the most frequent systemic findings in this study, potentially reflecting viral dissemination, immune-mediated inflammation, or multi-organ dysfunction. These observations are supported by Kumar VS et al., (2023), who also documented hepatosplenomegaly in paediatric AES cases [19].

In the current study, neurological examination revealed that 95% of children exhibited altered consciousness, with bilateral extensor plantar responses in 65%, brisk reflexes in 57.5%, and hypertonia in 41.25%. Additional findings included meningeal signs (12.5%), papilloedema (10%), focal deficits (2.5%), and ankle clonus (1.25%). These features reflect significant CNS involvement, commonly seen in AES due to inflammation, raised ICP, or diffuse neuronal injury.

In the present study, 8.75% of cases were attributed to viral pathogens, 31.25% to bacterial causes, while 60% remained undiagnosed. Goel S et al., (2017) reported over 100 potential pathogens, with viruses being predominant, such as JE, HSV, VZV, EBV, and Enteroviruses [20]. Kamble S and Raghvendra B (2016) found viral causes in 84.5% of AES cases, whereas Basu R and Kalamuddin MD (2018) and Srivastava N et al., (2022) highlighted a broad aetiological spectrum, including JE, bacterial meningitis, Acute disseminated encephalomyelitis (ADEM), cerebral malaria, and Orientia tsutsugamushi [21-23]. This variability underscores the diagnostic challenge and the need for comprehensive pathogen screening.

The present study evaluated average BDNF concentrations across different aetiologies of AES, revealing comparable levels: 23.23±8.34 in viral cases, 22.50±3.18 in bacterial cases, and 24.54±6.42 in cases of unknown origin. The lack of significant variation suggests BDNF may not be a reliable biomarker for differentiating AES aetiology. The uniformity across groups may reflect shared neuroinflammatory pathways involved in disease pathogenesis. Additionally, no correlation was observed between BDNF levels and clinical outcomes. While Costa HS et al., (2018) identified 2.5 ng/mL as a prognostic cut-off [24], and Morichi S et al., (2014) linked elevated BDNF with bacterial meningitis severity [12], the current study findings did not support BDNF as a prognostic or diagnostic indicator in AES. Nonetheless, its role in CNS inflammatory responses warrants further investigation.

Limitation(s)

Being conducted in a tertiary care setting, the findings may not be fully generalisable to the broader population. The absence of a control group, due to the ethical and logistical challenges of obtaining consent for lumbar puncture in non CNS cases-limited comparative analysis.

CONCLUSION(S)

The present study highlights the significant clinical burden of AES in children, with a high prevalence in those aged 5-12 years. Despite the critical role of BDNF in neuroinflammatory conditions, no significant changes in BDNF levels were observed across different aetiologies or patient outcomes in this cohort. While BDNF may not serve as a definitive biomarker for distinguishing AES causes or predicting outcomes, its potential therapeutic role warrants further investigation. The study also underscores the need for timely diagnosis, appropriate treatment, and better understanding of the pathophysiology of AES, particularly in terms of neuroinflammatory responses. Future research should focus on refining therapeutic interventions targeting BDNF and exploring other biomarkers to improve the prognosis of children with AES.

Authors' contribution: CK, SKP, NA, MV, SKS: Concept and design; SKP, CK, MV, NA, SKS: Acquisition, analysis, or interpretation of data; SKP, MV, CK, NA: Drafting of the manuscript; CK, MV, SKS, NA, SKP: Critical review of the manuscript for important intellectual content; CK, MV, SKS, NA: Supervision.

REFERENCES

[1] Baranwal SK, Hussain A, Paul S. Clinico-etiological profile and outcome of acute encephalitis syndrome in children. TCMS.2023;3(1): 289-94
[2] Misra UK, Kalita J. Changing spectrum of acute encephalitis syndrome in India and a syndromic approach. Annals of Indian Academy of Neurology. 2022;25(3):354-66.
[3] World Health Organization. Guidelines for Surveillance of Acute Encephalitis Syndrome. New Delhi: WHO Regional Office for South-East Asia; 2006.
[4] Rajeev S, Nishan K, Dipesh T, Tato Cristina M, Manu V, Vida A, et al. Investigation of acute encephalitis syndrome with implementation of metagenomic next generation sequencing in Nepal. BMC Infect Dis. 2024;24(1):734. Doi: 10.1186/s12879-024-09628-y. PMID: 39054413; PMCID: PMC11274775.
[5] Narain JP, Dhariwal AC, MacIntyre CR. Acute encephalitis in India: An unfolding tragedy. Indian Journal of Medical Research. 2017;145(5):584-87.
[6] The Times of India: Encephalitis to be made 'notifiable disease': Govt. [Jul; 2024]. 2016. http://timesofindia.indiatimes.com/city/delhi/encephalitis-to-be-made-notifiable-diseasegovt/articleshow/53651028.cms http://timesofindia.indiatimes.com/city/delhi/encephalitis-to-be-made-notifiable-disease-govt/articleshow/53651028.cms.
[7] Abdulkader RS, Ramasamy S, Vaman RS, Sapkal GN, Narayan J, Vijay N, et al. Acute encephalitis syndrome and Japanese encephalitis in India: insights from a nationally representative laboratory surveillance network, 2014–2023. BMC Infect Dis. 2026;26:989. https://doi.org/10.1186/s12879-025-12274-7.
[8] Reuben R, Gajanana A. Japanese encephalitis in India. The Indian Journal of Paediatrics. 1997;64:243-51.
[9] Cohen-Cory S, Kidane AH, Shirkey NJ, Marshak S. Brain-derived neurotrophic factor and the development of structural neuronal connectivity. Developmental Neurobiology. 2010;70(5):271-88.
[10] Barde YA. The physiopathology of brain-derived neurotrophic factor. Physiological Reviews. 2025;105(4). Doi: 10.1152/physrev.00038.2024.
[11] Bathina S, Das UN. Brain-derived neurotrophic factor and its clinical implications. Archives of Medical Science. 2015;11(6):1164-78.
[12] Morichi S, Yamanaka G, Ishida Y, Oana S, Kashiwagi Y, Kawashima H. Brain-derived neurotrophic factor and interleukin-6 levels in the serum and cerebrospinal fluid of children with viral infection-induced encephalopathy. Neurochemical Research. 2014;39:2143-49.
[13] Wurzelmann M, Romeika J, Sun D. Therapeutic potential of brain-derived neurotrophic factor (BDNF) and a small molecular mimics of BDNF for traumatic brain injury. Neural Regeneration Research. 2017;12(1):7-12.
[14] Reddy MN, Belavadi G, Priyanka VH. Study on acute encephalitis syndrome in children and their correlation with clinical parameters and etiological factors. International Journal of Contemporary Pediatrics. 2019;6(6):2628-33.
[15] Tripathy SK, Mishra P, Dwibedi B, Priyadarshini L, Das RR. Clinico-epidemiological study of viral acute encephalitis syndrome cases and comparison to nonviral cases in children from Eastern India. Journal of Global Infectious Diseases. 2019;11(1):7-12.
[16] Gogoi A, Panyang R, Baro L, Baruah A, Dowerah P. Acute encephalitis syndrome in children with special reference to Japanese encephalitis: A retrospective analysis. J Evol Med Dent Sci. 2016;5:3389-94.
[17] Santoso LA, Widodo DP, Munasir Z. Factors associated with outcome of acute encephalitis in children: A retrospective study of three referral hospitals. Medical Journal of Indonesia. 2020;29(2):154-63.
[18] Majhi SC, Nayak H, Murmu MC, Sahoo GR, Meher SK, Panda S, et al. Predictors of mortality in acute encephalitis syndrome in children. Panacea J Med Sci. 2024;14(1):229-36.
[19] Kumar VS, Sivasubramanian S, Padmanabhan P, Anupama CP, Ramesh K, Gunasekaran, P, Kitambi SS. Etiological profile and clinico epidemiological patterns of acute encephalitis syndrome in Tamil Nadu, India. Journal of Global Infectious Diseases. 2023;15(2):52-58.

[20] Goel S, Chakravarti A, Mantan M, Kumar S, Ashraf MA. Diagnostic approach to viral Acute Encephalitis Syndrome (AES) in paediatric age group: A study from New Delhi. J Clin Diagn Res. 2017;11(9):DC25-DC29.
[21] Kamble S, Raghvendra B. A clinico-epidemiological profile of acute encephalitis syndrome in children of Bellary. Int J Comm Med Public Health. 2016;3(11):2997-3002.
[22] Basu R, Kalamuddin MD. An epidemiological study on clinical profile and short term outcome in children of acute encephalitis syndrome in a tertiary care centre of west bengal with special reference to the various prognostic markers. IOSR J Dent Med Sci (IOSR-JDMS). 2018;17(2):14-19.
[23] Srivastava N, Deval H, Mittal M, Kant R, Bondre VP. The outbreaks of acute encephalitis syndrome in Uttar Pradesh, India (1978-2020) and its effective management: A remarkable public health success story. Front Public Health. 2022;9:793268.
[24] Costa HS, Lima MMO, Figueiredo PHS, Martinelli PM, Camargos ER, Chaves AT, et al. Prognostic value of serum brain-derived neurotrophic factor levels in patients with Chagas cardiomyopathy. Memorias do Instituto Oswaldo Cruz. 2018;113(10):e180224.

PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Paediatrics, Maharani Laxmi Bai Medical College, Jhansi, Uttar Pradesh, India.
2. Professor, Department of Paediatrics, King George's Medical University, Lucknow, Uttar Pradesh, India.
3. Assistant Professor, Department of Paediatrics, King George's Medical University, Lucknow, Uttar Pradesh, India.
4. Associate Professor, Department of Paediatrics, King George's Medical University, Lucknow, Uttar Pradesh, India.
5. Professor, Centre for Advanced Research (CFAR), King George's Medical University, Lucknow, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Manisha Verma,
Assistant Professor, Department of Paediatrics, King George's Medical University, Chowk, Lucknow-226003, Uttar Pradesh, India.
E-mail: manisha.verma.lko@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 04, 2026
- Manual Googling: Aug 01, 2026
- iThenticate Software: Aug 03, 2026 (6%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Feb 09, 2026**
Date of Peer Review: **May 19, 2026**
Date of Acceptance: **Aug 05, 2026**
Date of Publishing: **Nov 01, 2026**