Faridpur Med. Coll. J. 2025;20(2):07-12 DOI: https://doi.org/10.3329/fmcj.v20i2.82987

Original Article

Clinico-Etiological Profile of Acute Viral Encephalitis in Children of a Tertiary Care Hospital in Bangladesh

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Abstract:

Viral encephalitis, despite varying etiologies, often presents with similar clinical features, challenging clinicians in determining appropriate management strategies. This study aimed to investigate the etiological agents and associated clinical features of viral encephalitis in pediatric patients.

A multicenter observational cross-sectional study was conducted over 15 months at the Department of Pediatric Neurology, Bangladesh Medical University (BMU), and the Department of Pediatrics, Dhaka Medical College Hospital. Sixty-four children with acute encephalitis were enrolled based on inclusion and exclusion criteria. Detailed clinical history, physical examination, and cerebrospinal fluid (CSF) analyses, including biochemical, cytological, bacteriological, and Neuro-9 viral panel studies, were performed. Informed consent was obtained from guardians.

The mean age of participants was 4.10±3.87 years, with 59.4% aged ≤3 years. Varicella zoster virus (VZV) was the most frequently identified pathogen, present in 18.8% of cases, followed by Herpes Simplex Virus (HSV)-1 (3.1%) and Human Adenovirus (1.6%). No viral pathogen was identified in 76.5% of cases. Common presenting symptoms included fever (95.3%), seizures (87.5%), altered sensorium (85.9%), and prodromal symptoms (76.6%).

In this cohort, the etiology of acute viral encephalitis remained unidentified in the majority of cases. VZV was the predominant virus detected, followed by HSV-1 and Adenovirus. Fever, seizures, altered sensorium, and prodromal symptoms were the most frequent clinical features. Thorough clinical evaluation is crucial for guiding management and excluding other differential diagnoses.

Keywords: Acute encephalitis, Etiology, Clinical features, Children.

Introduction:

Acute encephalitis is a devastating infection of the central nervous system (CNS), often leading to severe morbidity and mortality, especially in children. The disease can be caused by a wide variety of pathogens, including bacteria, fungi, and parasites. However, viral infections are the most common and significant cause of encephalitis.[1] Viral encephalitis has an incidence rate ranging from 3.5 to 7.5 per 100,000 people, although

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this estimate may vary by region and over time due to changes in epidemiology and viral strains.[2]

While viral encephalitis is a global concern, its true incidence is likely underestimated, particularly in developing countries where diagnostics for pathogen detection are not always readily available.[1]

It is estimated that approximately 20,000 new encephalitis cases are diagnosed in Bangladesh annually[3]. Among those most commonly isolated viruses are Enteroviruses, Human Parechoviruses, Herpes Simplex virus (HSV) type 1 and 2. Other less common causes of viral encephalitis are Herpesviridae, Influenza, Arboviruses, Nipah virus, Rabies virus, and Japanese encephalitis virus (JEV).[2] A hospital-based study conducted at Mymensingh and Rajshahi Medical College Hospitals in 2003 found that 6% of patients tested positive for Japanese encephalitis, while 2% were positive for HSV5. In Bangladesh, there have been four major outbreaks of encephalitis, including episodes caused by Nipah or Nipah-like viruses in 2001, 2003, and 2004, which resulted in a high mortality rate of 25%. These outbreaks have heightened public and governmental concern regarding the management and prevention of viral encephalitis.[3]

The diagnosis of viral encephalitis requires a high degree of clinical suspicion.[4] Encephalitis causes neurologic dysfunction and has a broad range of presenting symptoms and signs. The clinical manifestations vary depending upon the viral agent, the affected region(s) of the brain, the age of the patient, and the patient's immune status.[5] In neonates and young infants, the clinical manifestations can be nonspecific, making diagnosis particularly challenging. In older children and adolescents, symptoms are often more pronounced, but identifying the exact viral cause remains difficult.

Identifying the etiology of encephalitis is challenging but essential for proper management and for saving lives. Etiology specific clinical profile is very sparse in our country; this study was done to detect the clinical features and etiologies of acute viral encephalitis in children.

Materials & Methods:

This multi-center cross sectional study was conducted in the department of pediatric neurology, Institute of Pediatric Neurodisorder and Autism (IPNA), Bangladesh Medical University (BMU) and Department of Pediatrics, Dhaka Medical College Hospital from December 2019 to February 2021. A 64 admitted children aged 1 month to 15 years, suspected as cases of acute encephalitis were enrolled in this study. Patients who were finally diagnosed as meningitis, febrile seizure or epilepsy, and patients in whom CSF sample collection was not possible were excluded from this study.

Children who had clinical features of encephalitis were enrolled in this study. After taking informed written consent from guardian of each child, detailed history was taken including demographic features like age, sex, residence and also presenting clinical features, like fever, seizure, altered consciousness, respiratory symptoms, GI symptoms, skin rash, headache etc. A thorough physical examination with special emphasis on neurological examination including level of consciousness, any sign of focal neurological deficit, seizure activity, movement disorder, eye examination findings like visual acuity, 6th nerve palsy, pupil, and papilledema was done. Then complete blood picture, blood culture, peripheral smear or RDT (Rapid Diagnostic Test) for malaria parasite (where applicable) was done. If there are features of raised intracranial pressure or suspicion of other diagnosis like autoimmune encephalitis, ADEM then neuroimaging (MRI) was done urgently before lumber puncture. EEG was also performed if needed. After excluding other diagnosis by initial tests, patients were finally enrolled. Within 24 hours of admission lumbar puncture (LP) was done with proper precaution and CSF was collected. From each patient, minimum 3 ml CSF was collected in 3 different tubes. After collection, CSF vacutainer tube was tightly sealed by cap and kept in vaccine career. The temperature of vaccine career was kept around 4°C by frozen cold pack and transported to the lab maintaining the cold chain. One tube was sent for RT-PCR in the department of Virology, BMU. At the same time another 2 tube was sent for cytology & biochemistry to the department of Microbiology and Biochemistry of respective institute. In the Department of Virology, BMU, CSF processing and the real-time multiplex PCR assay was performed on an ABI 7500 instrument (Life Technologies, USA) as per the manufacturer's instructions using the FTD Neuro-9 molecular detection (Fast Track Diagnostics, Luxembourg) containing lyophilized master mix, primer and probe mix for nine viruses (Herpes simplex virus type 1 & Herpes simplex virus type 2, Varicella Zoster virus, Human adenovirus, Epstein-Barr virus, Human cytomegalovirus, Human enterovirus, Human Parvovirus B19 and Human Parechovirus, Human Herpes virus 6 and 7). The admitted child was managed as per treatment protocol of the institution.

Data were collected using a pre-designed data collection sheet. Data were presented in tabulated form. Data were analyzed using computer-based program Statistical Package for Social Science (SPSS) for Windows version 23 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The qualitative observations were indicated by frequencies and percentages. Chi square test was done to determine the association between categorical variables. A p value <0.05 was considered as significant.

Results:

Among the 64 study cases more than half of the patients (59.4%) were aged between 1 month to 3 years. Mean (±SD) age of the study population was 4.10±3.87 years. Male were 61% and female children were 39%. Majority (64%) of the study population were from rural area (Table I).

Table I: Distribution of patients according to demographic profile (N=64)

Variable	Number (%)
Age (Means ± SD)	4.10 ± 3.87
<3 Years	59.40%
4-9 years	26.60%
10-15 Years	14.10%
Sex	
Male	39 (61%)
Female	25 (39%)
M:F	1.5:1
Residence	
Rural	41 (64%)
Urban	23 (36%)

The common presenting symptoms among the children were fever (95.3%), seizure (87.5%), altered consciousness (85.9%), skin rash (9.4%) and headache (6.25%). A large number of patients had respiratory prodromal symptoms (53.1%) including cough, runny nose, nasal stuffiness, and GI symptoms (20.3%) like nausea, vomiting, diarrhea.

The presenting signs among the study population were fever (84.4%), GCS <13 (53.1%), focal deficit (37.5%), neck rigidity (32.8%), aphasia (29.7%) who previously learnt to speak, visual defect (18.8%), hearing defect (12.5%) and hemiplegia (6.3%) (Table II).

Table II: Distribution of patients according to clinical parameters (N=64)

Variable	Number (%)
Clinical manifestation	
Fever	61 (95.3)
Seizure	56 (87.5)
Altered sensorium	55 (85.9)
Prodromal symptoms	49 (76.6)
Respiratory symptoms	34 (53.1)
GI symptoms	13 (20.3)
Skin rash	6 (9.4)
Headache	4 (6.25)
Presenting sign	
Raised Temperature	54 (84.4)
GCS <13	34 (53.1)
Focal deficit	23 (35.9)
Neck rigidity	21 (32.8)
Aphasia	17 (26.5)
Visual defect	11 (17.2)
Hearing defect	8 (12.5)
Skin Rash	6 (9.4)
Hemiplegia	4 (6.3)

The laboratory findings among the study cases revealed that an abnormal CBC finding was 67.2% and blood culture was positive in 3.1% of patients. In CSF study, cell count was <5/mm^3 in 31.3% of patients, 5-30/mm^3 in 50% and >30/mm^3 was in 18.8% of patients. Protein was <40 mg/dl in 21.9%, 40-80 mg/dl in 56.3% and > 80 mg/dl in 21.9% of patients. Sugar level was normal in 85.9% of patients and low in 14.1% of patients. Real time PCR was positive in 23.50% of patients. In 76.50% of patients, no definite virus was identified by neuro9 viral panel (Table III).

Table III: Distribution of patients according to laboratory parameters (N=64)

Investigations	Findings	Number (%)
Blood		
CBC	Normal	21 (32.8)
	Abnormal	43 (67.2)
Culture & sensitivity	Positive	2 (3.1)
	Negative	62 (96.9)

Malarial Parasite	Positive	1 (1.6)
	Negative	63 (98.4)
CSF Study		
WBC	<5 /mm^3	20 (31.3)
	5-30 /mm^3	32 (50)
	>30 /mm^3	12 (18.8)
Protein	<40 mg/dl	14 (21.9)
	40-80 mg/dl	36 (56.3)
	>80 mg/dl	14 (21.9)
Sugar	Low	9 (14.1)
	Normal	55 (85.9)
RT- PCR	Positive	15 (23.50)
	Negative	49 (76.50)

Viruses were identified in CSF study by using RT PCR Neuro9 viral panel among 64 study population, where Varicella Zoster Virus was isolated in 12 (18.8%) patients, Herpes Simplex 1 was found in 2 (3.10 %) patients and one (1.6%) patient had Human Adenovirus. No virus could be isolated in 76.5% patients **(Figure 1)**.

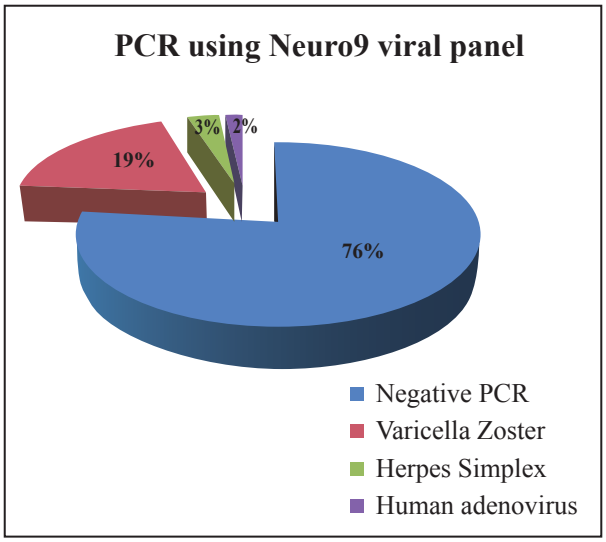

Figure-1: Isolated virus through Real Time PCR using Neuro9 viral panel among the study cases (N=64).

Discussion

Acute encephalitis is a significant public health concern due to its high morbidity and mortality rates, particularly in children. The clinical presentation of this condition is diverse, typically involving an acute onset of fever, altered mental status, and new-onset seizures, which are key diagnostic indicators. However, distinguishing viral encephalitis from other central nervous system (CNS) disorders can be challenging, leading to delays in diagnosis and treatment.[6] This is especially true in pediatric populations, where symptoms may overlap with other neurological diseases. The present study aimed to investigate the clinical and laboratory features of acute viral encephalitis in children to aid in better diagnosis and management.

In this study, 64 children aged less than 15 years were evaluated, with a mean age of 4.10±3.87 years. The majority of the patients (59.4%) were below three years of age, consistent with earlier findings by Mahmud et al[7] who reported a mean age of 3.77 years with a similar male predominance. Other studies, such as one by Halsey et al[8] also indicate a higher incidence of encephalitis in younger children, particularly those between the ages of 1 to 4 years. In the current study, male children comprised 61% of the sample, a finding that mirrors the 61% male predominance reported by Mahmud et al.[7] Additionally, most of the children (64%) were from rural areas, similar to the 75% rural population observed in Mahmud's study. These demographic findings are important as they highlight potential epidemiological patterns, suggesting that younger, male children from rural areas may be at higher risk for encephalitis.

Regarding clinical presentation, fever (95.3%), seizures (87.5%), and altered sensorium (85.9%) were the most common symptoms observed in the study population. This is in agreement with findings from several other studies[7] who reported fever (89%), seizures (84%), and altered sensorium (75%) as the most common symptoms. These symptoms are hallmark features of acute viral encephalitis and should raise immediate concern in pediatric cases. Neurological signs, such as neck rigidity (32.8%) and focal deficits (35.9%), were also prevalent in this study, which is comparable to findings by Mahmud et al[7] who reported neck rigidity in 17% of cases and focal deficits in 35.9%. Kakoti et al[9] also found meningeal irritation in 55.22% of cases, indicating that signs of meningeal involvement are common in encephalitis. Interestingly, respiratory symptoms (53.1%) and gastrointestinal symptoms (20.3%) were also observed in this study, consistent with Mahmud's findings[7] of respiratory prodromal features (34%) and gastrointestinal symptoms such as diarrhea (15%) and vomiting (28%). The lower incidence of headache (6.25%) in this study, compared to Kakoti et al.'s findings[9], may be attributed to the younger age group, where headache may be less frequently reported or recognized.

The cerebrospinal fluid (CSF) analysis plays a crucial role in diagnosing viral encephalitis. In this study, mild pleocytosis (5-30/mm³) was observed in 50% of patients, with protein levels mildly elevated (40-80 mg/dL) in over half of the cases, and hypoglycorrhachia (low CSF glucose levels) in 14.1% of cases. These findings align with those of Kenneth et al[10] who reported similar patterns of mild pleocytosis and elevated protein levels in encephalitis cases. However, it is important to note that a substantial proportion of patients may present with normal or only mildly abnormal CSF findings, making it difficult to rely solely on CSF analysis for a definitive diagnosis. Blood investigations revealed leukocytosis in 67.2% of patients, a common finding in encephalitis and other CNS infections, but blood cultures were positive in only 3.1% of cases, highlighting the need for more specific diagnostic tools.

Viral identification through real-time PCR revealed that 23.5% of patients had positive virus detection, with varicella-zoster virus (VZV) being the most commonly identified pathogen in 18.8% of cases. This contrasts with findings from other studies, where viruses such as Japanese encephalitis virus (JEV), enteroviruses, and herpes simplex virus (HSV) are more commonly detected. For instance, a study by Mori et al[11] in Bangladesh identified a wide range of viruses, including human bocavirus (HBoV1), mumps, and adenoviruses, without a clear predominance of any single pathogen. The variability in viral identification across studies may be due to differences in geographic regions, seasonal variations, and the availability of diagnostic tools. In the current study, the use of multiplex real-time PCR, which screened for only nine neurotropic viruses, may have limited the detection of other potential pathogens, such as JEV, Nipah virus, and rabies virus, leading to an underestimation of the true viral etiology.

The low virus yield (76.5% negative results) in this study is consistent with the findings of previous research, where viral identification rates are often low. Mori et al[11] identified organisms in only 18.5% of cases in a study conducted in Bangladesh. Negative results can be attributed to several factors, including the timing of CSF collection, as the sensitivity of PCR testing for certain viruses, such as HSV, is highest within 3 to 5 days of symptom onset. Additionally, the absence of diagnostic kits for some common pathogens may have contributed to the low detection rate. Despite these limitations, the identification of VZV as the most common virus in this study is noteworthy, as it suggests a potential shift in the viral landscape of encephalitis in this region.

In a nutshell, the findings of this study underscore the complexity of diagnosing and managing acute viral encephalitis in children. The clinical presentation, characterized by fever, seizures, and altered sensorium, remains consistent across studies, but the variability in viral identification highlights the need for improved diagnostic tools and broader screening capabilities. Early diagnosis and appropriate treatment are critical in reducing the morbidity and mortality associated with this condition, particularly in resource-limited settings where diagnostic and therapeutic options may be constrained. Further research is needed to explore the epidemiological patterns of encephalitis in different regions and to develop more effective strategies for prevention and management.

Conclusion:

The etiology of acute viral encephalitis in children remains unknown in most cases. Varicella zoster virus was the predominant virus followed by Herpes Simplex 1 and Adenovirus identified by Neuro9 viral panel in children with encephalitis. The most common symptoms were fever, seizures, altered sensorium and prodromal symptoms.

Conflict of interest:

There is no conflict of interest.

Acknowledgement:

Gratefully acknowledge the thoughtful comments of our teacher, colleagues. We are deeply grateful to those patients who sacrificed their valuable time and participated eagerly in our study.

References:

1. Anwar SS, Begum N, Khatoon S, Rashid R. Clinico-Pathological Profiles and Outcomes of Acute Viral Encephalitis in Children. *Bangladesh Journal of Infectious Diseases*. 2020; 7(1):8.

2. Hardarson SH. 'Acute viral encephalitis in children: Pathogenesis, incidence, and etiology', *Uptodate*. 2019; 1-16.

3. Hussain SM, Hossain MJ, Ekram AR, Gurley ES, Alam MM, Montgomery SP, et al. Preliminary report of encephalitis surveillance study in Rajshahi Medical College Hospital. TAJ: *Journal of Teachers Association*. 2004;17(2):75-9.

4. Alcaraz AR, Lu-Bolanos M, Gonzales ML. Clinical profile and outcomes in acute viral encephalitis. *Pediatr Infect Dis Soc Phil J*. 2016;17(2):37-46.

5. Hardarson, SH. Acute viral encephalitis in children and adolescents: Clinical manifestations and diagnosis ‘, *Uptodate*. 2019:1–38

6. Sharma S, Mishra D, Aneja S, Kumar R, Jain A, Vashishtha VM, Expert Group on Encephalitis, Indian Academy of Pediatrics. Consensus guidelines on evaluation and management of suspected acute viral encephalitis in children in India. *Indian pediatrics*. 2012; 49:897-910.

7. Mahamud NU, Barua SK, Chowdhury PK, Karim MR, Barua PC, Kamal AH. Clinical and Epidemiological Profile of Paediatric Encephalitis Patients in a Tertiary Care Hospital. *Bangladesh Journal of Child Health*. 2014 ;38(1):5-10.

8. Committee on Infectious Diseases. Varicella vaccine update. *Pediatrics*. 2000;105(1):136-41.

9. Kakoti G, Dutta P, Das RB, Borah J, Mahanta J. Clinical profile and outcome of Japanese encephalitis in children admitted with acute encephalitis syndrome. *BioMed research international*. 2013; 2013(1):152656.

10. Swaiman KF, Ashwal S, Ferriero DM, Schor NF, Finkel RS, Gropman AL, Pearl PL. *Swaiman's pediatric neurology e-book: Principles and practice*. Elsevier Health Sciences; 2017; 16:895-906.

11. Mori D, Khanam W, Sheikh RA, Tabib SSB, Ikebe E, Hossain MM, et al. Increased serum vascular endothelial growth factor is associated with acute viral encephalitis in Bangladeshi children, *Scientific reports*. 2017; 7(1):1-7.