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Original Research Article

Clinical, Radiological, and Electrophysiological features of Viral Encephalitis: a clue towards an Etiological Diagnosis

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Abstract:

Background: Viral encephalitis is a neurological emergency with varied clinical manifestations and often delayed etiological confirmation. Recognition of characteristic clinical, radiological, and electrophysiological patterns can assist in early presumptive diagnosis and management.

Objectives: To evaluate the clinical presentation, magnetic resonance imaging (MRI), and electroencephalographic (EEG) features of viral encephalitis and identify patterns suggestive of specific viral etiologies.

Methods: This prospective observational study was conducted at a tertiary care center in northern India from January to November 2025. Forty-eight patients with clinically and/or radiologically suspected viral encephalitis were evaluated. All patients underwent detailed clinical assessment, MRI brain, EEG, and cerebrospinal fluid analysis, with etiological confirmation attempted using PCR or serology wherever feasible.

Results: The mean age was 34.7 ± 19.2 years, with male predominance. Fever (100%) altered sensorium (91.7%), and seizures (70.8%) were the most common clinical features. Based on MRI, limbic involvement was the most frequent radiological pattern (37.5%), followed by cortical (27.0%) and thalamic (18.75%) patterns. EEG abnormalities were classified as focal (29.2%) or diffuse (70.8%). Focal EEG abnormalities were significantly associated with identification of a specific viral etiology ($p = 0.0049$). HSV-1 was the most common identified virus, while a substantial proportion remained etiologically unidentified.

Conclusion: Integration of clinical features with MRI and EEG provides valuable etiological clues in viral encephalitis and facilitates early diagnosis and timely management.

Keywords: Viral encephalitis, MRI, EEG, HSV, Japanese encephalitis, PLEDs.

Introduction

Viral encephalitis is a major cause of acute febrile encephalopathy worldwide and represents a significant neurological emergency. It contributes substantially to morbidity and mortality and is frequently associated with long-term neurological sequelae among survivors [1,2]. The clinical presentation is diverse; fever, altered sensorium, seizures, behavioral changes, and focal neurological deficits are all common manifestations. This variability reflects differences in viral neurotropism, host immune response, and the regional distribution of cerebral involvement [3,4]. Despite advances in neurovirology, establishing a definitive etiological diagnosis remains challenging in routine clinical practice. Molecular diagnostic techniques, including polymerase chain reaction (PCR), and serological assays are not universally available and may be time-consuming. Moreover, diagnostic yield can be influenced by the timing of cerebrospinal fluid sampling and prior antiviral therapy, potentially resulting in false-negative results [5,6]. These challenges are particularly pronounced in resource-limited settings, where clinicians are often required to initiate treatment based on clinical suspicion rather than confirmed etiological evidence.

Magnetic resonance imaging (MRI) is the most sensitive modality for detecting parenchymal involvement in suspected viral encephalitis. Certain imaging patterns may suggest specific etiologies. Medial temporal and insular involvement, often with thalamic or basal ganglia lesions, is characteristic of herpes simplex virus (HSV) encephalitis, whereas Japanese encephalitis and other arboviral infections more commonly involve the thalami and deep gray nuclei [7–9]. Dengue and other emerging viral

infections may demonstrate variable cortical and subcortical lesions [10]. Electroencephalography (EEG) is a useful adjunct for identifying seizures and assessing cortical dysfunction. Diffuse slowing on electroencephalography (EEG) reflects global cerebral dysfunction, whereas periodic lateralized epileptiform discharges (PLEDs), strongly associated with herpes simplex virus (HSV) encephalitis, indicate severe focal cortical involvement [11,12]. When interpreted alongside MRI findings, EEG patterns can substantially aid early etiological suspicion and diagnostic narrowing. Recognition of characteristic clinical, imaging, and electrophysiological features enables timely initiation of targeted antiviral therapy and supportive care, which are critical for improving survival and neurological outcomes [13–15].

In endemic regions such as northern India, where multiple neurotropic viruses coexist and access to advanced diagnostics may be limited, a multimodal diagnostic approach is particularly important. This study aims to evaluate the clinical, MRI, and EEG features of patients with viral encephalitis at a tertiary care center and to identify characteristic patterns that may facilitate early etiological inference prior to laboratory confirmation.

Materials and Methods

Study Design and Setting: This study was a prospective observational study conducted in the Department of Neurology at Himalayan Hospital, Swami Rama Himalayan University, Dehradun, Uttarakhand, India. The period of study was from January 2025 to November 2025.

Study Population

During the study period, the patients presenting with clinical features compatible with viral encephalitis were screened and included in the study. A total of 48 patients meeting the inclusion criteria were enrolled in the study after being informed and obtaining consent from patients or their legally authorized representatives.

Inclusion Criteria: Patients were included if they presented with acute febrile encephalopathy characterized by fever, altered level of consciousness, seizures, or behavioral changes, with or without focal neurological deficits, and neuroimaging findings on brain MRI suggestive of encephalitis.

Exclusion Criteria: Patients with confirmed bacterial, tubercular, or fungal meningitis were excluded. Those with non-viral central nervous system infections, brain tumors, metabolic encephalopathy, or autoimmune encephalitis were also excluded. Additionally, patients with contraindications to MRI (e.g., non–MRI-compatible cardiac pacemakers, metallic implants, neurostimulators, or severe claustrophobia) were not included in the study.

Clinical Assessment: All participants underwent comprehensive clinical evaluation at admission. Demographic data and detailed clinical information—including duration of illness, seizure semiology, level of consciousness assessed using the Glasgow Coma Scale (GCS), and focal neurological deficits—were recorded. A complete neurological examination was performed in all cases, and the in-hospital clinical course was documented.

Neuroimaging: Brain magnetic resonance imaging (MRI) was performed using a 1.5-Tesla scanner. Sequences included T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR), diffusion-weighted imaging (DWI), and susceptibility-weighted imaging (SWI). Images were systematically evaluated for lesion location, laterality, and patterns of involvement, including the temporal lobes, thalami, basal ganglia, cortical–subcortical regions, and brainstem.

Electroencephalography: All patients underwent a standard 30-minute scalp electroencephalography (EEG) recording using the international 10–20 system. Recordings were analyzed for background activity, diffuse or focal slowing, epileptiform discharges, periodic lateralized epileptiform discharges (PLEDs), and other abnormal patterns. EEG interpretations were performed by an experienced neurologist blinded to the patients' clinical diagnosis.

Cerebrospinal Fluid Analysis: Lumbar puncture was performed in all patients without contraindications. Cerebrospinal fluid (CSF) was analyzed for total and differential cell counts, protein concentration, and glucose levels. Etiological evaluation included reverse transcription polymerase chain reaction (RT-PCR) and/or serological testing for herpes simplex virus (HSV), Japanese encephalitis virus (JEV), dengue virus (DENV), varicella-zoster virus (VZV), and cytomegalovirus (CMV), as clinically indicated and subject to resource availability.

Etiological Classification: Etiological diagnoses were confirmed when commercial serological assays or viral PCR tests were positive. In cases where these tests were not performed or negative, but MRI and EEG findings were strongly suggestive, etiological classification was based on characteristic radiological features and clinical presentation.

Statistical Analysis: Information was entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 25. For continuous variables, mean ± standard deviation was used, and for categorical variables, frequency and percentage were used. The relationship between clinical,

radiological, and electrophysiological findings was examined and measured using the appropriate statistical tests. A p-value of less than 0.05 was used to define statistical significance.

Ethical Considerations: The study received approval from the Institutional Ethics Committee of Himalayan Hospital, Dehradun. All participants or legal guardians provided written informed consent prior to study enrollment.

Results

Demographic Characteristics: Among the 48 patients who had viral encephalitis, the average age of study participants was 34.7 years, with a standard deviation of 19.2 years, ranging from adolescent to older adults. In the demographic study, the males predominated, 28 (58.3%) males and 20 (41.7%) females, with a male to female ratio of 1.4:1.

Table 1: Demographic profile of the study population

Variable	Value
Total patients	48
Mean age (years)	34.7 ± 19.2
Male	28 (58.3%)
Female	20 (41.7%)
Male: Female ratio	1.4:1

Clinical Presentation: All participants (100%) had fever. Among the 48 patients, 44 (91.7%) had altered sensorium, the most common neurological manifestation. Seizures were reported in 34 (70.8%) patients. 25 (52.1%) patients reported headaches. 17 (35.4%) patients had focal neurological deficits. 11 (22.9%) patients had behavioral abnormalities.

Table 2: Clinical features at presentation

Clinical feature	Number of patients (%)
Fever	48 (100)
Altered sensorium	44 (91.7)
Seizures	34 (70.8)
Headache	25 (52.1)
Focal neurological deficit	17 (35.4)
Behavioral changes	11 (22.9)

Radiological and Electroencephalographic Correlation: A total of 48 patients with acute viral encephalitis were evaluated during the one-year study period. Based on MRI brain findings, radiological patterns were classified into five categories: limbic, cortical, thalamic, ganglionic, and normal imaging. Limbic involvement was the most frequently observed pattern, seen in 18 patients (37.5%), followed by cortical involvement in 13 patients (27.0%). Thalamic lesions were identified in 9 patients (18.75%), while ganglionic involvement and normal MRI findings were observed in 4 patients (8.3%) each.

Electroencephalographic findings were categorized into focal and diffuse abnormalities. Overall, 14 patients (29.2%) demonstrated focal EEG abnormalities, whereas 34 patients (70.8%) showed diffuse EEG abnormalities.

When radiological patterns were correlated with EEG findings and final etiological diagnosis, limbic involvement was predominantly associated with focal EEG abnormalities and was most commonly linked to herpes simplex virus infection. Cortical and thalamic patterns showed a higher proportion of diffuse EEG abnormalities and were frequently associated with dengue virus, Japanese encephalitis virus, or remained etiologically unspecified. Ganglionic involvement was mainly associated with diffuse EEG abnormalities. Patients with normal MRI also predominantly demonstrated diffuse EEG abnormalities.

These associations are summarized in **Table 3**, which illustrates the distribution of radiological patterns, EEG abnormalities, and diagnostic categories.

Table 3: Radiological patterns on MRI and their correlation with EEG abnormalities and etiological diagnosis

MRI Pattern	Number	Etiological Diagnosis	EEG Finding
Thalamic	9	4 = Dengue 2 = JE 1 = VZV 2 = Unspecified	Focal ABN = 1 Diffuse ABN = 8
Cortical	13	5 = Specific (Dengue, HSV, VZV) 8 = Unspecified	Focal ABN = 1 Diffuse ABN = 12
Ganglionic	4	2 = dengue 2= unspecified	Diffuse ABN = 4
Limbic	18	11 = HSV 7 = Unspecified	Focal ABN = 12 Diffuse ABN = 6
Normal	4	4 = Unspecified	Diffuse ABN = 4
Total	48	Specific = 25 Unspecified = 23	Focal ABN = 14 Diffuse ABN =34

Further analysis demonstrated a strong relationship between EEG abnormality type and etiological yield. Among patients with focal EEG abnormalities, 12 out of 14 patients (85.7%) had a specific viral etiology identified. In contrast, only 14 out of 34 patients (41.2%) with diffuse EEG abnormalities had a confirmed viral diagnosis. This difference was statistically significant ($p = 0.0049$), indicating that focal EEG abnormalities are highly predictive of identifying a specific viral etiology (**Table 4**).

Table 4: EEG findings and associated etiologies

EEG Finding	Number	Diagnosis	P value
Focal Abnormality	14	Specific = 12 Unspecified = 2	0.0049
Diffuse Abnormality	34	Specific = 14 Unspecified = 20	

Etiological Diagnosis: Out of the 48 patients, 26 (54.2%) had confirmed aetiology. The most frequently identified virus was the herpes simplex virus 1 (HSV-1) in 13 patients (27.1%). Dengue virus was identified in 8 (16.6%) patients, Japanese encephalitis virus in 3 (6.2%), while varicella zoster virus was identified in 2 (4.1%). In 22 patients (45.8%), an aetiological agent could not be determined despite thorough workup

Table 5: Etiological distribution of viral encephalitis

Etiological agent	Number (%)
HSV-1	13 (27.1)
Dengue virus	8 (16.6)
Japanese encephalitis virus	3 (6.2)
Varicella-zoster virus	2 (4.1)
Unidentified	22 (45.8)

Discussion

This study highlights the diagnostic value of integrating clinical presentation with magnetic resonance imaging (MRI) and electroencephalography (EEG) findings in patients with viral encephalitis. The findings are particularly relevant in settings where rapid etiological confirmation is not feasible. Viral encephalitis continues to pose significant diagnostic challenges due to its nonspecific clinical manifestations and the variable sensitivity of laboratory investigations. These limitations underscore the importance of adjunctive diagnostic modalities to support timely clinical decision-making [16].

In this cohort, fever, altered sensorium, and seizures were the most frequently reported clinical manifestations, consistent with findings from studies conducted in other endemic regions [17]. These features, indicative of diffuse cerebral involvement, emphasize the need for prompt neuroimaging and electrophysiological evaluation in all cases of febrile encephalopathy. Temporal and insular lobe involvement was the most common radiological pattern and showed the strongest association with herpes simplex virus (HSV) encephalitis. This observation is well documented and likely reflects the virus's propensity to spread along the limbic system, resulting in focal cortical

necrosis and hemorrhagic inflammation. The presence of periodic lateralized epileptiform discharges (PLEDs) on EEG further supports the diagnosis of HSV infection, as these discharges represent a hallmark of focal cortical irritation characteristic of HSV encephalitis [18,19].

Dengue-related encephalitis and Japanese encephalitis showed predominantly bilateral thalamic and basal ganglia involvement. Radiologically, thalamic involvement has been classically described and corresponds to the virus's preference for deep gray matter nuclei in Japanese encephalitis [20]. More recently reported, dengue encephalitis has cortical–subcortical changes and overall EEG slowing, corroborating the awareness of this virus as neurotropic and not solely systemic [21].

Diffuse background slowing on EEG was the most common electrophysiological abnormality in our series. Although nonspecific, such slowing reflects global cerebral dysfunction and has been associated with greater disease severity and poorer outcomes in encephalitis [22]. In contrast, focal epileptiform discharges were less frequent and were most commonly observed in varicella-zoster virus infection, consistent with its tendency to cause multifocal cortical involvement and vasculopathy [23].

Although a strict diagnostic protocol was followed, nearly 50% of patients in this series remained without a confirmed etiological diagnosis. This is a finding that has also been documented in extensive encephalitis surveillance studies that show 40 to 60% of cases remain without identified etiology, even after extensive evaluations [24]. Possible explanations include limited diagnostic panels, emerging or novel pathogens, immune-mediated mechanisms, and suboptimal timing of molecular testing resulting in false-negative results. The findings of this study emphasize that while laboratory confirmation remains the gold standard, clinico-radiological and electrophysiological correlations provide valuable etiological clues that can guide early therapeutic decisions. Such an approach is particularly relevant in resource-limited settings, where delays in definitive diagnosis may significantly impact clinical outcomes [25].

Conclusion

Viral encephalitis demonstrates characteristic clinicoradiological and electrophysiological patterns that, when interpreted collectively, provide valuable etiological clues. Involvement of the temporal and insular lobes on the MRI and the presence of periodic lateralized epileptiform discharges on the EEG are strong predictors of herpes simplex virus encephalitis, while bilateral thalamic lesions favor Japanese encephalitis. Dengue-related encephalitis more commonly presents with diffuse cortical and subcortical involvement, and generalised EEG slowing. Although laboratory confirmation remains the diagnostic gold standard, integration of clinical features with MRI and EEG findings can facilitate early etiological suspicion and timely initiation of targeted therapy. This approach is particularly relevant in endemic and resource-limited settings, where delays in definitive laboratory diagnosis may adversely affect neurological outcomes.

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