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Original Research Article

# Neurological Manifestations of Dengue Fever in Adults: A Prospective Study from Eastern India

**Ashok Kumar Singh[1], Satyam Kumar[2]**

[1]Assistant Professor, Department of General Medicine, Jawahar Lal Nehru Medical College & Hospital, Bhagalpur, Bihar, India

[2]Junior Resident (Academic), Department of General Medicine, Jawahar Lal Nehru Medical College & Hospital, Bhagalpur, Bihar, India

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**Corresponding Author: Dr. Ashok Kumar Singh**

**Conflict of interest: Nil**

**Abstract**

**Background:** Prior reports of dengue'sneurological involvement included an encephalopathy mostly brought on by protracted shock, hyponatremia, and liver failure. The virus's direct neurotropic potential was recently identified. The purpose of this study was to document the neurological complications of dengue fever infection in adults.

**Method:** 100 consecutive adult dengue fever patients were included in a prospective, cross-sectional study to document neurological sequelae and carry out a thorough clinical and laboratory evaluation. From January 1, 2024, to August 31, 2024, these individuals were admitted to the intensive care unit (ICU) or medicine ward of Jawahar Lal Nehru Medical College & Hospital in Bhagalpur, Bihar, India. Version 22.0 of the SPSS program (IBM Corp., Armonk, NY, USA) was used to conduct the appropriate statistical analysis.

**Results:** Of the 100 study adults with dengue fever, 10 adults (10%) had neurological complications. According to WHO 2009classifications of these patients included severe dengue fever (n = 7, 70%), those with warning indications (n = 2, 20%), and those without warning signs (n = 1, 10%).The cohort had a male-to-female ratioratio of 2:1 and an average age of 39.6 years. 60% (n = 6) of the patients presented with dengue fever and neurological involvement. Fever was (100%, = 10) was the most prevalent symptom, followed by headache (70%, n = 7), altered sensorium (60%, n = 6), seizure (60%, n = 6), vomiting (50%, n = 5), abdominal pain (40%, n = 4), arthralgia (10%, n = 1). Hepatomegaly (100%, n = 10), exaggerated deep tendon reflexes (80%, n = 8), puffiness (60%, n = 6), petechiae (40%, n = 4), lymphadenopathy (20%, n = 2), papilloedema (20%, n = 2), rash (20%, n = 2), splenomegaly (10%, n = 1), muscle tenderness (10%, n = 1), and cranial nerve palsy (10%, n = 1) were the most prevalent symptoms.

**Conclusion:** In adult, dengue feverrarely causes neurological problems. To stop more problems and death, however, prevention, early detection, and prompt therapeutic action are necessary.

**Keywords:** Dengue; Neurological Manifestations.



## Introduction

In many tropical and subtropical regions of the world, dengue fever, a virus spread by mosquitoes, remains a major public health concern [1]. The dengue virus (DENV), which has four different serotypes (DENV-1 to DENV-4), is the cause of the illness. From mild dengue fever (DF) to severe symptoms including dengue hemorrhagic fever (DHF), dengue shock syndrome (DSS), and expanded dengue syndrome (EDS), it can take many different clinical forms [2]. In recent decades, dengue has become much more common worldwide, with severe cases causing significant morbidity and mortality. The various clinical symptoms of dengue, especially its neurological, hematological, radiological, and cardiac consequences, remain poorly understood despite a great deal of research. Numerous neurological consequences, including as encephalitis, myelitis, and Guillain-Barré syndrome, have been linked to dengue; however, little is known about the frequency and features of these complications across various dengue clinical presentations [3]. Similarly, more research is required to determine how dengue affects hepatic and renal functioning as well as hematological parameters like platelet count, leukocyte count, and coagulation factors. Additionally underreported are radiological findings in dengue, such as abnormalities on ultrasonography and MRI [4]. The Ministry of Health and Family Welfare (MoHFW) of the Government of India has developed a number of programs, such as the National Vector Borne

Disease Control Programme (NVBDCP), to diagnose and control these diseases in India. Additionally, the Department of Health Research (DHR) has developed funding for the establishment of the Viral Research and Diagnostic Laboratory (VRDL) network [5]. The National Institute of Virology (NIV), Pune, occasionally offers recommendations for the identification of viral illnesses [6]. All teaching hospitals set up BSL-II RT-PCR facilities, which are comparable to VRDL, during the coronavirus disease 2019 pandemic, expanding the nation's ability to screen for viral diseases.

This study was aimed to document the neurological symptoms caused by dengue fever in adults admitted to a medical college hospital located in a rural area. This was done in light of the high morbidity and mortality rates linked to dengue infection as well as the dearth of research done in our nation's rural areas.

## Methods

100 consecutive adult dengue fever patients were included in a prospectiveobservational study to document neurological sequelae and carry out a thorough clinical and laboratory evaluation. From January 1, 2024, to August 31, 2024, these individuals were admitted to the intensive care unit (ICU) or medicine ward of Jawahar Lal Nehru Medical College & Hospital in Bhagalpur, Bihar, India. Version 22.0 of the SPSS program was used to conduct the appropriate statistical analysis. Adults who had dengue fever-like symptoms and had positive serological testing for the dengue-specific NS1 antigen, IgG, and IgM antibodies were included in the study. Inclusion age cut-off was ≥18 years. Subjects who had negative dengue serological testing and parental rejection were not included.

Every patient underwent a thorough clinical evaluation that included a history taking, a clinical examination, and pertinent laboratory tests, such as complete blood counts with hematocrit, blood sugar, liver and renal function tests, prothrombin and activated partial thromboplastin times, electrolytes, electrocardiograms, chest radiography, and abdominal ultrasound. Commercial kits based on quick solid phase immunochromatography were used to qualitatively identify dengue-specific NS1antigen, IgG, and IgM antibodies.

All study individuals were grouped according to the 2009 WHO criteria for dengue fever as:

- Severe Infection/fever;
- Fever/infection with warning signs;
- Fever/infection without warning signs

A pre-tested proforma was used to document all neurological signs and symptoms that were seen in the study participants either during hospitalization or at the time of admission. Patients with encephalopathy, encephalitis, or acute disseminated encephalomyelitis had computed tomography or magnetic resonance imaging of the brain and spinal cord in addition to a thorough study of their cerebrospinal fluid. S. As needed, electromyography (EMG), fundus examination, muscle biopsy, nerve conduction velocity (NCV), and CPK levels were carried out. In addition to a systemic examination that supports dengue infection and the identification of NS1, IgG, and IgM antibodies for dengue in a serum sample, the following diagnostic criteria were taken into consideration for this investigation.

Version 22.0 of the SPSS program was used to conduct the appropriate statistical analysis. The Institution's Ethics Committee granted permission to conduct this study.

## Results

Of the 100 study adults with dengue fever, 10 subjects (10%) had neurological complications (Figure 1).

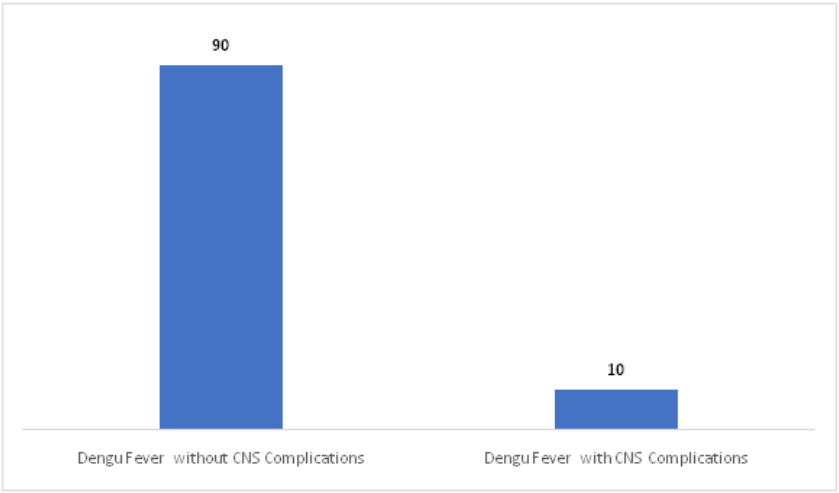


**Figure 1: Number of dengue fever patients with / without neurological complications**

According to WHO 2009 classifications of these patients included severe dengue fever (n = 7, 70%), those with warning sings (n = 2, 20%), and those without warning signs (n = 1, 10%). The cohort had a male-to-female ratio of 2:1 and an average age of 39.6 years. 60% (n = 6) of the patients presented with dengue fever and neurological involvement were aged more than 30 years. Fever (100%, = 10) was the most prevalent symptom (Figure 2), followed by headache (70%, n = 7), altered sensorium (60%, n = 6), seizure (60%, n = 6), vomiting (50%, n = 5), abdominal pain (40%, n = 4) and, arthralgia (10%, n = 1).

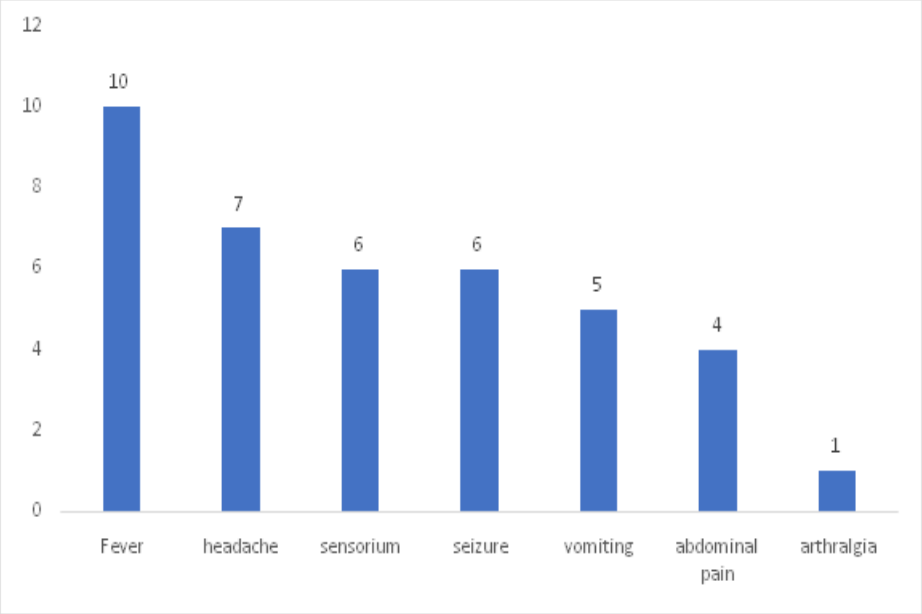


**Figure 2: Common symptoms in study subjects with neurological complications**

Hepatomegaly (100%, n = 10), exaggerated deep tendon reflexes (80%, n = 8), puffiness (60%, n = 6), petechiae (40%, n = 4), lymphadenopathy (20%, n = 2), papilloedema (20%, n = 2), rash (20%, n = 2), splenomegaly (10%, n = 1), muscle tenderness (10%, n = 1), and cranial nerve palsy (10%, n = 1) were the most prevalent symptoms (Figure 3).

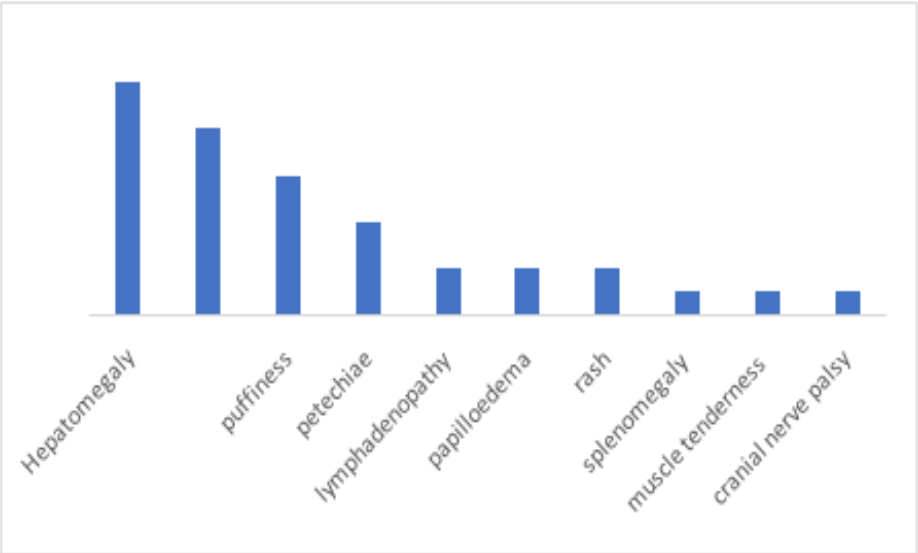


**Figure 3: Common signs in study subjects with neurological complications**

Table 1 displays the neurological issues and CT/MRI brain results that were noted in the research participants. Some patients had multiple manifestations.

**Table 1: Neurological manifestations of participants**

| Neurological manifestations | No. of cases N=10 (%) | CT / MRI Brain findings | No. of deaths |
|---|---|---|---|
| Encephalopathy | 5 (50%) | Normal (n=3, 60%)<br>Extensive involvement of b/l cerebellar region, brainstem and thalami with peculiar rim enhancement (n = 2, 25%) | 1 |
| Encephalitis | 3 (30%) | Normal (n = 2, 60%)<br>Cerebral edema (n = 1, 40%) | 0 |
| Myositis | 2 (20%) | Normal | 0 |
| Acute disseminated encephalomyelitis | 1 (10%) | Hyperintense white matter lesions on T2-weighted images in centrum semiovale, corona radiata and corpus callosum | 1 |
| Hemiplegia with facial nerve palsy | 1 (10%) | Hypodensity (ischemic infarct) in right parietal lobe in cranial CT scan | 0 |
| Intracranial haemorrhage | 1 (10%) | Hyperdensity in frontal lobe in cranial CT scan | 0 |

## Discussion

In tropical and subtropical regions of the world, dengue has a significant morbidity and fatality rate among subjects [7]. Although the 2009 WHO Guidelines defined severe dengue as involving the central nervous system, the new guidelines do not include standardized case definitions or diagnostic criteria for "neuro-dengue"[8]. In 1976, neurological manifestations were initially documented as unusual dengue infection symptoms, with incidence rates ranging from 0.5 to 20% in several study groups that included adult patients [8–12]. The overall incidence in this study was 10%.

Neurological problems were found to be substantially more common in severe dengue cases (n = 8, 80%). In research participants we assessed in more detail the neurological syndromes seen most frequently in the patients with a CT/MRI test, namely encephalopathy [5(50%)], Encephalitis [3 (30%)], Myositis [2 (20%)], Acute disseminated encephalomyelitis [1 (10%)], hemiplegia with facial nerve palsy [1 (10%)] and intracranial haemorrhage [1 (10%)]. Approximately half of our patients with dengue infection with CNS presentations had encephalopathy.

The neurological symptoms observed in our study, such as fever (100%), headache (70%), altered sensorium (60%), seizure (60%), and meningeal signs (10%), underscore the neurotropic potential of dengue virus. Similar studies have also reported significant neurological involvement in dengue patients. For instance, Solomon et al. (2000) identified headache, altered sensorium, and seizures as common neurological manifestations in dengue patients [14].Seven patients (70%) out of ten instances with neurological symptoms in this study had secondary dengue, making them at risk of developing severe dengue. Neurological changes in dengue infection can happen in three different ways [10,14]. The most frequent side effect linked to shock and multi-organ failure in the research participants was encephalopathy. This is consistent with Oehler et al.'s findings [12]. The dengue virus was initially thought to be non-neurotropic. Recent research, however, has shown that it is invasive and can cross the blood-brain barrier in experimental animal models, particularly when it comes to serotypes 2 and 3 [17–18]. The most frequent neurological complication of dengue, encephalopathy and encephalitis, have been documented to occur in 0.5% to 6.2% of cases. Dengue associated encephalopathy is generally very serious, with around 50% of the affected patients succumbing [13]. Clinicians should be knowledgeable of the expanded dengue syndrome characterized by the concurrent compromise of cardiac, neurological, gastrointestinal, renal, and hematopopoietic systems. Isolated cranial nerve palsies occur rather uncommonly and are often steroid responsive. These neuropathies may result from the direct involvement of cranial nerve nuclei or nerve involvement or may be immune-mediated. Even if the diagnosis of dengue is confirmed, it is absolutely imperative to exclude other well-known causes of isolated cranial nerve palsies. Ischemic and hemorrhagic strokes may occur following dengue fever.

Given that the condition is widespread, one of the study's strengths was the large number of patients it included. However, due to financial and resource limitations, the ELISA approach could not be used for dengue serology or for the detection of dengue-specific IgM in CSF. Furthermore, it was not possible to conduct comprehensive investigations to rule out other potential viral etiologies. In areas where dengue is endemic, the presence of suggestive clinical symptoms may lead to a diagnosis of neurological abnormalities secondary to dengue.

## Conclusion

Dengue can cause neurological problems that are common and can affect nearly every aspect of the nervous system through a variety of different

methods. Presenting these findings is specifically intended to raise awareness of the numerous neurological complications that dengue frequently cause in adults, particularly in developing countries where access to diagnostic methods is restricted.

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