

## Clinical Profile of Dengue, Clinical Manifestations And Its Neurological Involvement.

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**Abstract:** Dengue fever has a wide geographical distribution, and can present with a diverse clinical spectrum. Recent observations indicate that the clinical profile of dengue is changing, and that neurological manifestations are being reported more frequently. The exact incidence of various neurological complications is uncertain. This study is undertaken to evaluate common modes of clinical presentation and neurological complications in our hospital and correlate these features with lab findings which may help us in early diagnosis and better case management to reduce mortality. Results were analysed and discussed. In conclusion, critically ill children with dengue may have varied manifestations. Most complications such as established and refractory shock, diastolic dysfunction, abdominal compartment syndrome, DIC, ARDS were more frequent in severe established shock. Neurological events, for the most part, were unrelated to the perfusion status.

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### I. Introduction

Dengue fever is an arthropod borne viral fever. Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas. The incidence of dengue has grown dramatically around the world in recent decades. Over 2.5 billion people – over 40% of the world's population are now at risk from dengue. WHO currently estimates there may be 50–100 million dengue infections worldwide every year. An estimated 500 000 people with severe dengue require hospitalization each year, a large proportion of whom are children. About 2.5% of those affected die. [1-4] Earlier it was prevalent in those areas with humid atmosphere and plenty of rain. It is vital to recognize at the earliest- the signs and symptoms, alteration in biochemical parameters and multisystem involvement pattern in dengue to reduce the mortality.

It has a wide geographical distribution, and can present with a diverse clinical spectrum. Recent observations indicate that the clinical profile of dengue is changing, and that neurological manifestations are being reported more frequently. The exact incidence of various neurological complications is uncertain. [5] Pathogenesis of the neurological manifestations is multiple and include neurotrophic effect of the dengue virus related to the systemic effects of dengue infection and immune mediated. There are various neurological manifestations including seizure, encephalopathy, meningitis, myelitis, Guillain-Barré syndrome (GBS), and myoclonus that are commonly reported. [6,7] In the last few years, numerous neurological complications related to dengue fever (DF) have been reported and these lead to significant morbidity and mortality. Neurological complications occur in 0.5-6% of cases with DF. [8] Systemic complications resulting in encephalopathy, stroke, hypokalemic paralysis, postinfectious immune-mediated acute disseminated encephalomyelitis and myositis have also been reported in some studies. [9,10]

This study is undertaken to evaluate common modes of clinical presentation and neurological complications in our hospital and correlate these features with lab findings which may help us in early diagnosis and better case management to reduce mortality.

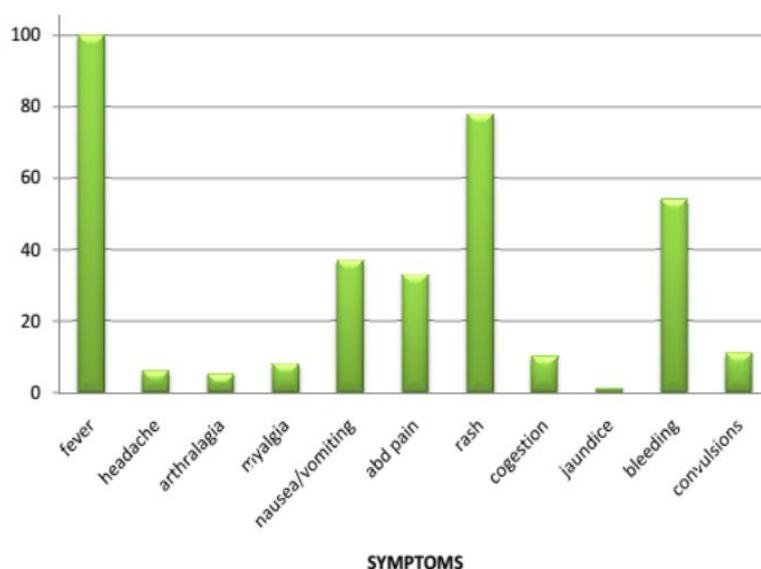
### II. Methodology

All the children admitted with clinical features suggestive of Dengue and who were diagnosed serologically with IgM and IgG levels during 2009-2011 were included in the study. A total of 200 patients were included in the study. Cases that tested positive for dengue IgM antibodies were classified into dengue fever, dengue hemorrhagic fever and dengue shock syndrome as per WHO criteria. The baseline characteristics, including age, sex, occupation, and socioeconomic class, were noted. A detailed history, clinical evaluation, and detailed neurological examination were performed in all the patients. The muscle power was recorded and noted according to the Medical Research Council grading system. Systemic complications of DF including jaundice, lymphadenopathy, hepatosplenomegaly, cardiac failure, gastrointestinal, respiratory, and hematological manifestations were specifically examined. The routine laboratory investigations including hemoglobin level,

blood count, platelet estimation, hematocrit, blood sugar, liver function test, renal function test, creatine kinase, prothrombin time, activated partial thromboplastin time, and electrolytes were performed in each patient. The ELISA for human immunodeficiency virus (HIV) was performed in all the patients. Electrocardiogram and chest radiography were done in all the patients. Cerebrospinal fluid (CSF) analysis, and computed tomography (CT) scan and magnetic resource imaging (MRI) of the brain were performed in patients in whom neurological complications were seen.

### III. Result

Mean age of the group was 5.8 years (range 3-12) with 55% of them being females and 45% males. Average stay in hospital was 6.8 days. Of the 100 dengue seropositive cases 29% cases are dengue shock syndrome, 16% are dengue hemorrhagic fever and 55% are dengue fever. Fever was the manifestation in 100% of the cases, whereas the other most common manifestations are enumerated in Figure 1 that depicts the symptomatology percentage in the affected population of the study group.



**Fig 1 : Percentage of population having the symptomatology.**

Seizure was seen in 9(4.5%) patients, six of them were diagnosed as DF, and the rest as DHF-I. Papilledema was seen in six (3.00%) cases, and all of them had neurological abnormalities. Meningeal signs like neck rigidity and Kernig's signs were positive in three (01.5%) cases, and both of these were under the category of DF. In two (1%) cases, focal neurological deficit was seen, which was categorized as DHF. Oliguria was reported in 5.7% of the patients. In all the patients of neurological complications, CSF analysis was done; in four patients, cell counts were raised with lymphocytic predominance, sugar was normal, but protein was markedly raised and they were diagnosed as cases of viral meningitis. The most common neurological manifestation was seizure, seen in nine patients (4.5%), followed by encephalopathy and meningitis, both seen in 4 patients (2%) of DF. In two patients (1%), intracranial hemorrhage was seen. None of them were associated with either DHF or DSS. Meningitis was present in four (2%) cases of DF; none of them were associated with either DHF or DSS. Nine (4.5%) patients presented as cases of generalized tonic-clonic seizure (GTCS), four of them (2%) were having associated encephalopathy, while in six patients (3%) seizure was an independent presentation. Out of the nine patients presented with seizures, six (3%) were suffering from DF and three patients (1.5%) were diagnosed as cases of DHF. Two patients (1%) presented as having an intracranial hemorrhage; these patients presented with focal neurological deficit. Both these cases were diagnosed as DHF

### IV. Discussion

Dengue infection, from being a sporadic illness, has now become a regular post-monsoon. Involvement of children and increase in the frequency of the epidemic are indicators of higher incidence of this infection. In the present study, the average age of presentation was 5.16 years, which suggests that the endemicity of dengue fever is on the rise. Fever, hypotension, vomiting, abdominal pain, hepatomegaly, thrombocytopenia, erythematous rash, bleeding manifestations in the form of malena, deranged aPTT and PT were the common clinical and laboratory features. Of the 100 dengue seropositive cases 29% cases are dengue shock syndrome,

16% are dengue hemorrhagic fever and 55% are dengue fever. Since this was a hospital-based study, it does not reflect the burden of the community infection of dengue that may just have no symptoms or undifferentiated fever. Thus, we had higher number of patients with DSS and DHF rather than the ones with undifferentiated fever. The community infection of DF is characterized by the 'iceberg' or 'pyramid' phenomenon. At the base most of the cases are symptomless, followed in increasing rarity by DHF and DSS. Thus, one can postulate from the study that since most of our patients had DHF and DSS, and being the tip of the iceberg, the base formed by undifferentiated fever may be very high, and thus the endemicity of dengue in the community would be quite high.

Fever was seen in 100% of patients infected though it was found that patients with milder disease (DF and dengue hepatitis) had longer duration of fever as compared to patients with severe dengue (DHF and DSS) who had shorter duration of fever, suggestive of the fact that secondary infection may lead to a more fulminant course due to antibody-dependent enhancement and that repeat infection may be more dangerous. With this increasing endemicity of dengue and rise in the prevalence of dengue in children, it is only a matter of time that dengue will become a major public health problem. The neurological complication in dengue infection has been hypothesized through pathogenic mechanisms concerned with neurotropism, leading to encephalitis, meningitis and myelitis, and systemic complications, thereby resulting in encephalopathy, stroke, and hypokalemic paralysis, and postinfections like immune-mediated acute disseminated encephalomyelitis (ADEM), GBS, and optic neuritis.[ 11] Encephalopathy may be due to hyponatremia, cerebral edema, and microvascular frank hemorrhage. The exact incidence and types of neurological manifestations in dengue have not been reported. Various discrete data are available regarding neurological illness in dengue. The patients presented with encephalitis-like illness in DF who may have normal cerebrospinal fluid findings except mildly increased cerebrospinal fluid protein. It can masquerade as other types of acute viral encephalitis. However, its clinical course and prognosis are usually favourable.[12] Among the CNS manifestations of DF, seizure is an important symptom presented and it is one of the most common neurological manifestations of DF.[13]

While children with DSS may have abnormal neurology secondary to cerebral hypoperfusion on account of shock leading to hypoxicischemic events and/or intracranial bleeds, other significant reasons for neurological presentations include cerebral edema, direct neurotropic effect of dengue virus resulting in encephalitis/encephalopathy, or secondary to hepatic dysfunction and metabolic derangements such as hypoglycemia and hyponatremia.[14-17] Cranial imaging and CSF analysis were normal in the majority. 2 patients had clinical and MRI features suggestive of ADEM. While ADEM may occur following many viral exanthems and Guillain Barre syndrome has been described in Indian children following dengue infection, there has been only a single previous report on the occurrence of ADEM following dengue fever in an adult. [18]

## V. Conclusion

In conclusion, critically ill children with dengue may have varied manifestations. Most complications such as established and refractory shock, diastolic dysfunction, abdominal compartment syndrome, DIC, ARDS were more frequent in severe established shock. Neurological events, for the most part, were unrelated to the perfusion status.

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