

## STUDY OF CLINICAL PROFILE AND EARLY PREDICTORS OF MORTALITY IN DENGUE IN A TERTIARY CARE CENTRE IN CHENNAI

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### Abstract

**Background:** One of the seven nations in the Southeast Asia region that have been recognized as consistently reporting dengue fever (DF)/dengue hemorrhagic fever (DHF) outbreaks is India. Thus, the study aimed to identify early bleeding risk, hemodynamic instability and significance of APTT and platelets to prevent mortality and preventive strategies for dengue myocarditis-related complications and conduction abnormalities. **Material & Methods:** This prospective observational study was conducted from September 2022 to March 2023 on 306 patients. Demographic data like age, gender and address were recorded on predesigned and pretested proforma. Detailed medical history of patients, detailed clinical examination and distribution of symptoms were collected. Investigations like CBC, coagulation profile (PT, INR, APTT), RFT, LFT with enzymes, Chest X-ray, ECG, USG abdomen and pelvis were done during their stay in the hospital and outcomes were observed. **Results:** Around 66% (210 of 306) of people aged between 12-30 years were infected and admitted, with males (64%) being infected more than females (36%). Fever was the most common presenting complaint, followed quickly by fever, myalgia, vomiting and loose stools, headache, and abdominal pain and vomiting. Thrombocytopenia was seen in 68.7% of the cases. The leucocyte count was normal in most cases (61%), and leucopenia was observed in 39%. Liver function tests were normal in 63% of cases and deranged in 37%. Bleeding manifestations included hematemesis, gum bleeding, Malena and Menorrhagia. **Conclusion:** Although bleeding signs were seen in those with severe thrombocytopenia and extended APTT, those with severe thrombocytopenia and normal APTT did not.

## INTRODUCTION

Dengue is a systemic viral infection transmitted between humans by infected *Aedes* mosquitoes. *Aedes aegypti* and *Aedes albopictus* mosquitoes transmit this tropical viral fever.<sup>[1]</sup> The female *Aedes* mosquito gets infected with the dengue virus after a blood meal from an infected person during the febrile phase. With more than one-third of the world's population living in areas at risk for infection, the dengue virus is a leading cause of illness and death in

the tropics and subtropics. The burden of dengue in India is large; an estimated 33 million infections occur in India each year, with the potential for further spread and contributing to a third of the total global dengue burden, thereby warranting the need for this epidemiological study.<sup>[1,2]</sup>

Dengue cases are increasing in India, where there were 6.34 cases per million people between 1998 and 2009 and 34.81 cases per million people between 2010 and 2014. Dengue fever can present in various ways, ranging from fatigue and malaise during the

viral prodrome to shock and multiorgan failure syndrome during a severe illness. Less research has been done on the outcomes of dengue fever patients admitted to critical care units. Uncertainty persists regarding the prognostic factors that affect the clinical fate of severely ill dengue fever patients.<sup>[1,3-5]</sup> Thus, the study aimed to identify early bleeding risk, hemodynamic instability and significance of APTT and platelets to prevent mortality and preventive strategies for dengue myocarditis-related complications and conduction abnormalities.

## MATERIALS AND METHODS

This prospective observational study was conducted from September 2022 to March 2023 on 306 patients. The study received Institutional Ethical Committee approval before the initiation of the study. All participants' informed consent was obtained before their inclusion in the study.

### Inclusion Criteria

Patients of both sexes, aged above 12 years, who were admitted to medicine wards with IgM/IgG DENGUE and Dengue Ns1 positive, and patients who were transferred to IMCU owing to complications were included.

### Exclusion Criteria

The paediatric population aged below 12 years, pregnant ladies with Dengue fever in obstetric wards with fever with thrombocytopenia where Dengue (IgM, IgG, NS-1) were negative were excluded.

### Methods

Demographic data like age, gender and address were recorded on predesigned and pretested proforma. Detailed medical history of patients, detailed clinical examination and distribution of symptoms were collected. Investigations like CBC, coagulation profile (PT, INR, APTT), RFT, LFT with enzymes, Chest X-ray, ECG, USG abdomen and pelvis were done during their stay in the hospital and outcomes were observed.

The WHO classifies DHF in four grades (I to IV). The DHF grades I and II represent relatively mild cases without shock, whereas grades III and IV are more severe and accompanied by shock. The WHO defines dengue shock syndrome (DSS) as DHF plus signs of circulatory failure manifested by rapid and weak pulse, narrow pulse pressure ( $\leq 20$  mmHg) or hypotension for age, prolonged capillary refill, cold and clammy skin, and restlessness. Initial infection with a particular serotype (the primary infection) is usually asymptomatic or results in mild disease manifestations. However, subsequent infection (secondary dengue infections) may lead to severe disease that manifests in DHF/DSS.

### Statistical Methods

Microsoft Word and Excel were used to generate graphs, tables, etc., and the Chi-square test was used to study the association of platelets and APTT. Categorical variables were expressed in the frequency and percentages.

## RESULTS

### Disease of Young

Around 66% (210 of 306) of people aged between 12 years to 30 years were infected and admitted, with males 196 patients (64%) being infected, more than females 110 patients (36%) because females approach health care more than males and males spend more time outside than females and awareness among males is better than females. Fever was the most common presenting complaint, followed quickly by fever, myalgia, vomiting and loose stools, headache, and abdominal pain and vomiting (Table 1).

Thrombocytopenia in complete blood count is the most common reason for presentation/referral from PHCs. Hemoconcentration with an increase in the hematocrit of 20% or more is definitive evidence of increased vascular permeability and plasma leakage. Out of the 306 admitted patients, patients transferred to IMCU were as follows. Males 44% (196), accounting for 22%, and females 36 (110), accounting for 31% [Table 2].

Thrombocytopenia ( $<1,00,000/\text{mm}^3$ ) is a defining criterion for dengue haemorrhagic fever and was seen in 68.7% of the cases.

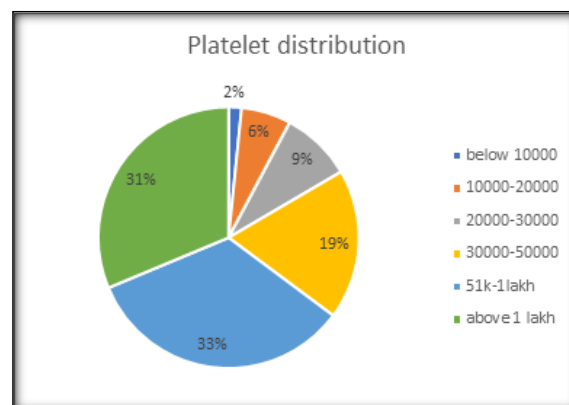


Figure 1: Distribution of platelet

Dengue infection, as per current observations, in our epidemiological locality, contrary to expectations, did not have much impact on the total leucocyte count. The leucocyte count was normal in most cases (61%), and leucopenia was observed in 39%. Liver function tests were normal in 63% of cases and deranged in 37% [Table 3].

Out of 306 patients, 234 (77%) had normal APTT and 72 (23%) patients had raised APTT (more than two times the control value). The 234 patients with a normal APTT, with a platelet count of over 10,000, had no bleeding manifestations.

Of the 72 patients with platelets above 20,000, 34 had bleeding manifestations, and 20 had no bleeding tendency. Of patients with platelets below 20000, 13 had bleeding manifestation, and 5 had no bleeding tendency (Table 4). Bleeding manifestations included hematemesis, gum bleeding, Malena and Menorrhagia [Table 4].

The bleeding manifestation was seen in most patients whose platelet count dropped below 20,000/mm<sup>3</sup>. However, it was also seen in patients whose platelet count was more than 50,000/mm<sup>3</sup>, mostly attributable to deranged APTT. Of 306 patients, 40.5% were admitted on the first day of afebrile period, followed by the second day (26.5%) and the third day (14.7%) [Table 5].

Among 306 patients, 28.8% had platelet falls on day 4, followed by 27.5% of patients who had platelet falls on the third day of the illness. Table 6 shows the percentage and number of patients who had platelet falls on their corresponding day of illness [Table 6]. Of 306 patients, four died: two died of viral myocarditis, one died of massive hematemesis, and one died of intracranial haemorrhage.

**Table 1: Distribution of symptoms**

Symptoms	No of patients	Percentage
Only fever	70	22
Fever with myalgia	76	24
Fever with vomiting	92	30
Fever with loose stools	27	8.8
Fever, vomiting, abdominal pain	26	8.4
Fever with headache	41	13

**Table 2: Hematocrit range**

Hematocrit range	No of pts	% of pts	IMCU transferred (% out of no. of pts)
20-30	9	2.9	2 (22)
30-35	37	12	20 (54)
35-40	92	30	34 (36)
40-45	111	36	14 (12.6)
45-50	40	13	4 (10)
Above 50	10	3.3	4 (40%)

**Table 3: Total count and liver function test**

Total count	Percentage	
	Below 4000	38.8
Liver function tests	4-10K	56.5
	Above 10K	4.5
	Deranged/elevated	37

**Table 4: Platelet range**

Platelet range	Bleeding	No bleeding tendency
Below 20000	13	5
20000-30000	11	4
30000-50000	15	7
Above 50000	8	9

**Table 5: Afebrile day % distribution**

Afebrile day	Afebrile day % distribution
Day 0	13.7
Day 1	40.5
Day 2	26.5
Day 3	14.7
Day 4	3.26
Day 5	1.3

**Table 6: Day of platelet fall**

Day of platelet fall	Percentage of patients	Number of patients
Day 1	7.51	23
Day 2	6.2	19
Day 3	27.5	84
Day 4	28.8	88
Day 5	16.6	51
Day 6	8.16	25
Day 7	2.9	9
Day 8	1.6	5
Day 9	0.6	2

## DISCUSSION

Outbreaks of dengue fever are frequent in tropical and subtropical regions worldwide. Its epidemiology

is evolving, and its incidence has significantly increased over the past few decades. Most symptomatic people have a minor illness, although complications can result in death. In the monsoon

season, it is one of the frequent causes of acute febrile sickness. An area of ongoing study has been identifying clinical and laboratory indicators that may identify patients at risk of the poorest outcome. Most of the literature has concentrated on laboratory indicators forecasting dengue fever severity rather than death.<sup>[6,7]</sup> It is more common among young people because they spend more time outdoors and are more exposed to mosquito bites. As per epidemiological study, young people from this study also tend to work and dwell in crowded urban areas. This study raises important questions about why the host response to Dengue virus varies by age and requires further exploration. The death rate per case was 8.7%. According to studies from various parts of the world, it has varied between 1.1% and 14%.<sup>[8,9]</sup> The variation may be caused by the higher proportion of patients in some trials who had problems upon presentation and the calibre of care they received. Up to 21% more patients died when receiving intensive care.<sup>[5]</sup>

In the current study, out of the 306 admitted patients, 44% (196) males (accounting for 22%) and 36% (110) females (accounting for 31%) patients were transferred to IMCU. This is supported by Caruso et al., who suggest that the biological appearances between males and females are based on immunological, hormonal/genetic factors determining susceptibility to disease and clinical outcome. Females mount a more vigorous response, owing to estrogen mounting the innate/adaptive immune response compared to males.<sup>[10]</sup>

Infected individuals with narrow pulse pressure and tachycardia should be advised strict bed rest (advised not to use toilets). Complications during the critical phase/afebrile period, like postural hypotension, viral myocarditis, and happy shock (hypovolemic shock due to plasma leakage, since a patient can walk around without showing severe symptoms) were settled after advising strict bed rest, fluid management and Inotrope support.

Dengue infection, as per current observations, in our epidemiological locality, contrary to expectations, did not have much impact on the total leucocyte count. The leucocyte count was normal in most cases (61%), and leucopenia was observed in 39%. Leukopenia is a common finding in dengue fever patients, and it has been connected to how serious the condition is. Non-survivors reportedly had a noticeably greater WBC at the presentation time, according to Thein et al. and Almas et al.<sup>[11,12]</sup> The presence of leukocytosis in dengue fever patients should alert the attending physician to potential consequences.

People with severe thrombocytopenia and normal APTT did not show any bleeding manifestations, but people with severe thrombocytopenia and prolonged APTT had bleeding manifestations. A common test result of dengue illness is thrombocytopenia. Bhaskar et al. from India have observed increased mortality among patients with thrombocytopenia (20,000/mcL) upon presentation.<sup>[9]</sup> In contrast, this

study found no link between thrombocytopenia at presentation and mortality. Thein et al., Karunakaran et al., and Khalil et al. made comparable observations.<sup>[11,13,14]</sup>

Researchers have disagreed on using ALT to predict dengue fever cases' outcomes. We discovered that the result was unaffected by acute liver damage at admission. Similar findings have been made by Thein et al.<sup>[11]</sup> and Karunakaran et al.<sup>[13]</sup> Still, they differ from those published by Almas et al., Huang et al., and Padyana et al., who said that hepatitis increases the risk of death from dengue fever.<sup>[12,15,5]</sup> The work addresses the crucial issue of identifying factors influencing dengue fever patients' mortality, which can help guide clinical judgment and enhance patient outcomes.

## CONCLUSION

This study identified the risk factors for mortality in dengue fever patients. The most frequent initial complaint was a fever, rapidly followed by myalgia, vomiting and loose stools, headache, and abdominal pain and vomiting. Although bleeding signs were seen in those with severe thrombocytopenia and extended APTT, those with severe thrombocytopenia and normal APTT did not. Additional investigation is required to uncover possible risk variables and create a more precise set of predictors for mortality in dengue fever patients.

### Limitations

Paediatric population aged below 12 years Pregnant ladies in obstetric wards were not included, and strains of dengue were not studied.

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