

## A Clinico-microbiological study of dengue fever cases at Sri Siddhartha medical college and hospital, Tumkur

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### Abstract

**Background:** Dengue is currently the second most prevalent vector borne disease in the world. Dengue fever and its more serious forms, dengue hemorrhagic fever and dengue shock syndrome, are becoming important public health problems. Since there is no immune prophylactic or specific antiviral therapy available, clinico-microbiological diagnosis plays a vital role in patient management and implementation of control measures.

**Objective:** To study the clinical and laboratory profile of Dengue cases admitted at Sri Siddhartha Medical College and Hospital.

**Materials and Methods:** A hospital based prospective study was carried out from June to December 2015 in Sri Siddhartha Medical College and Hospital. 150 seropositive cases aged between 18-75 years admitted in the medical wards were included. Clinical profile of the patients was noted. Rapid immunochromatography test and ELISA was performed to detect NS1 antigen, IgM and IgG antibodies. Platelet count, total leucocyte count and routine laboratory investigations were also analysed.

**Results & Discussion:** Out of 150 seropositive cases, 88 were males and 62 were females. The commonest presenting symptom was fever. In majority of cases thrombocytopenia ranged from 50,000 – 100,000/cu.mm. NS1 antigen, IgM and IgG antibodies were found Seropositive in 70%, 7%, and 3% cases respectively. In remaining 20% of cases, more than one marker was seropositive.

**Conclusion:** High degree of clinical suspicion, supported by laboratory evidences like thrombocytopenia and specific dengue serological tests help in early diagnosis of dengue.

**Keywords:** Dengue, clinical profile, IgM, IgG, NS1

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-5478.2016.00047.9

### Introduction

Dengue is an endemic arboviral disease worldwide. According to estimates of the World Health Organization (WHO), around two fifths of the world's population in tropical and subtropical countries are at constant risk of contracting this infection.<sup>1</sup>

In India; Dengue is a major public health problem and a leading cause of hospitalization. The number of dengue cases has increased over the last three to five years and is spreading to new areas. Previously it was considered to be a disease of the urban and the semiurban areas, but now it has started affecting the affluent class as well causing a major public health concern. The transmission of dengue occurs more in monsoon and post monsoon.<sup>2</sup>

Recurring outbreaks of Dengue fever have been reported from states like Andhra Pradesh, Delhi, Goa, Haryana, Gujarat, Karnataka, Kerala, Maharashtra, Rajasthan, Uttar Pradesh, Pondicherry, Tamil Nadu and West Bengal. The case fatality has increased to above 1% in last 10 years.<sup>3</sup>

Dengue is an acute, life threatening viral infection transmitted through the bite of infected Aedes mosquitoes, mainly Aedes aegypti. It is caused by four serotypes of dengue virus, namely DEN-1, DEN-2, DEN-3 and DEN-4 belonging to genus Flavivirus and family Flaviviridae. Serious manifestations occur more frequently in reinfections.<sup>3</sup>

Infection with any dengue virus serotype may manifest with a wide spectrum ranging from asymptomatic infection to an undifferentiated fever, classical dengue fever, and severe forms of the disease like Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS). After an incubation period of 2–7 days, patients present with sudden onset of fever, headache, backache, retro orbital pain and severe myalgia. Other common symptoms include anorexia, nausea or vomiting, marked cutaneous hypersensitivity. After 3-4 days of onset of fever, epistaxis, gingival and gastrointestinal bleeding and a maculopapular rash beginning on the trunk and spreading to the extremities and the face can appear. DHF is characterized by onset of dramatic haemorrhagic manifestations. DSS is most severe form of DHF that is due to significant intravascular volume depletion, haemodynamic compromise poor organ and tissue perfusion.<sup>4,5</sup>

The precise diagnosis of dengue infection can be achieved through viral isolation, viral RNA detection through RT-PCR, but these two methods are time consuming and costly. Hence Rapid

immunochromatography test and ELISA are performed to detect NS1 antigen, IgM and IgG antibodies.<sup>3</sup>

Platelet count is the only accessory test for diagnosis of dengue in periphery centres. Thrombocytopenia was more consistently associated whenever NS1 antigen was detected.<sup>6,7</sup>

Thus early clinical diagnosis and laboratory profile is important for patient management and is crucial in saving lives. The present study is an attempt to describe the salient clinical as well as laboratory findings of serologically confirmed hospitalized cases of dengue fever.

### Materials and Methods

The study was undertaken as a hospital-based prospective study between June to December 2015 in Sri Siddhartha Medical College and Hospital, Tumkur, Karnataka. 150 seropositive dengue fever cases of age group 18-75 years admitted in the medical wards were included in the study. Ethical clearance was obtained prior to the study and written informed consent was obtained from the participating patients.

Patients were evaluated for signs and symptoms including fever  $\geq 38^{\circ}\text{C}$ , headache, retro bulbar pain, myalgia, joint pain, anorexia, nausea/vomiting, maculopapular rash and bleeding manifestations. Complications like hypotension, pleural effusion, pneumonia, renal failure, ARDS, encephalopathy at any stage of dengue fever were noted.

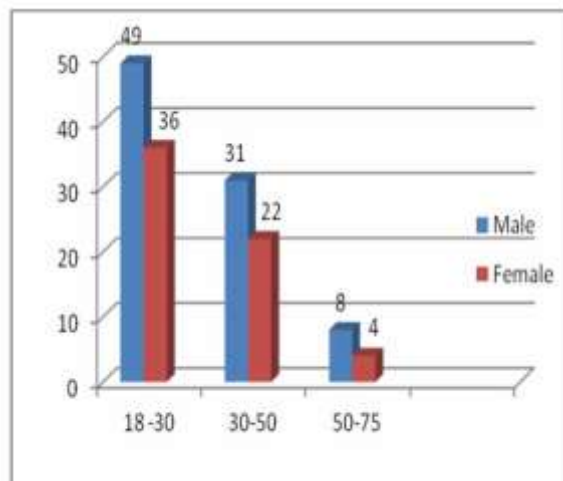
Blood samples were collected from patients. Serological testing was carried out using the "Dengue day 1 test kit (J. Mitra & co. Pvt. Ltd.)" which is a rapid visual test for Dengue NS1 Antigen, IgM and IgG Antibodies detection.

The samples testing positive for NS1 Ag and/or IgM antibodies by the rapid test were processed by the confirmatory NS1 Ag Microlisa, IgM Capture ELISA and IgG Capture ELISA kits (J. Mitra & co. Pvt. Ltd.). All the tests were performed as per the kit manual.

Routine laboratory tests such as complete hemogram, liver function test, renal function test, serum electrolytes and urine microscopy test were also done. Serial platelet count and hematocrit levels were monitored during the hospital stay. Radiological and other investigations were done when clinically warranted.

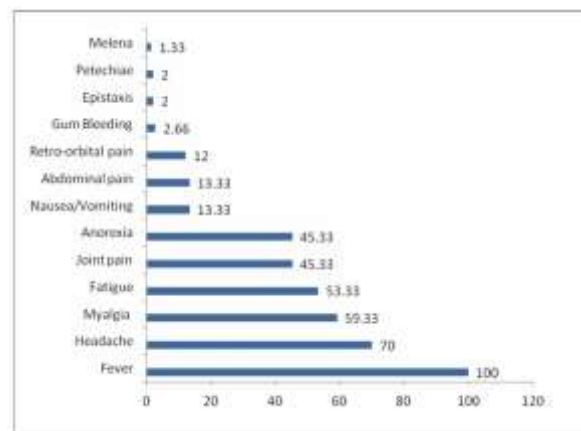
### Results

Out of 150 seropositive cases, 88 were males and 62 were females. 56.7% cases were observed in 18-30 years age group (**Fig. 1**). Most of the patients were from rural areas adjacent to Tumkur City, People who are working outdoor and spending more time outside home were more affected.

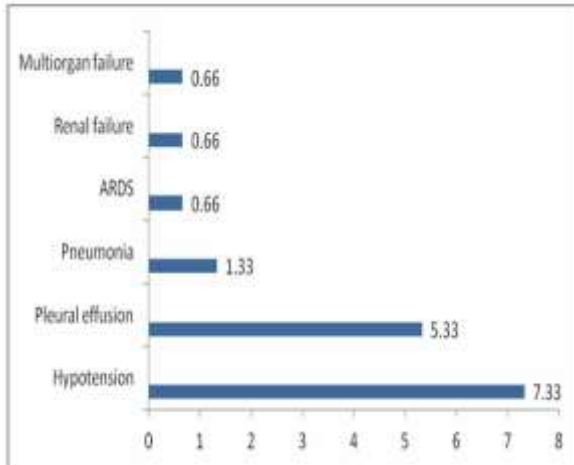


**Fig. 1: Age and sex distribution**

Fever was the commonest presenting symptom (100%), followed by severe headache, myalgia and fatigue. 14 patients (9.6%) had bleeding manifestations in the form of gum bleeding, epistaxis, hematuria and melena (**Fig. 2**). 24 patients (16%) developed various complications like hypotension, pleural effusion, pneumonia, ARDS, renal failure and multi-organ failure (**Fig. 3**).

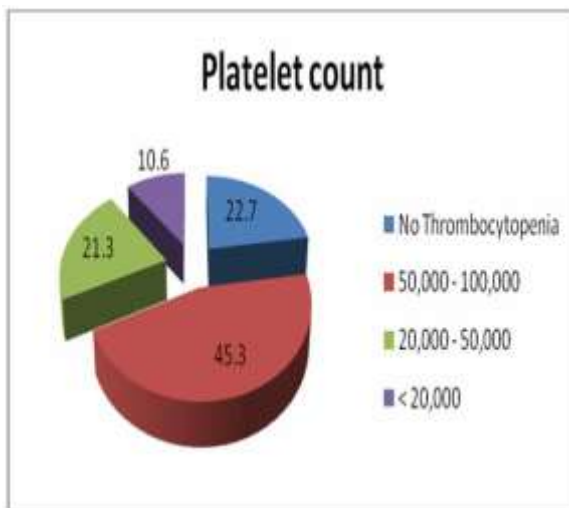


**Fig. 2: Distribution of clinical manifestations of Dengue fever in percentage**



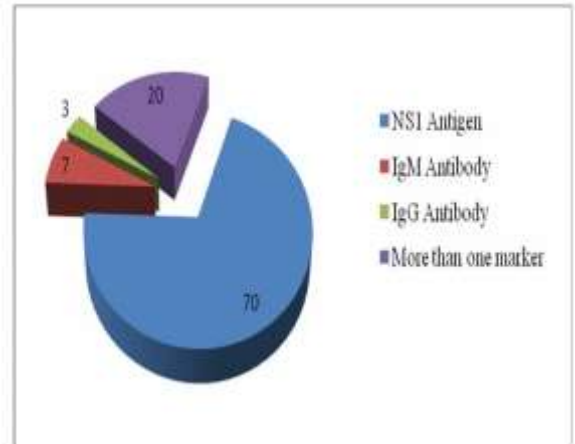
**Fig. 3: Distribution of the complications in percentage**

Thrombocytopenia (platelet count below 100,000/cu.mm) was the major haematological abnormality (77.2%) (Fig. 4). Leukopenia (total white blood cell count <4000/cu.mm) was seen in 53.3% cases. Elevated Hematocrit levels (>40) was observed in 62% cases. SGOT (>40u/l) was found raised in 30% of cases where as SGPT (>40u/l) in 27 % cases.



**Fig. 4: Distribution of Thrombocytopenia**

The distribution of various dengue specific parameters by ELISA is as shown in Fig. 5. Out of 150 cases, 70% were seropositive for NS1 antigen, 7% were seropositive for IgM antibodies and 3% were seropositive for IgG antibodies. In remaining 20% cases, more than one parameter was seropositive. In more than one marker seropositive samples, 11% (NS1 + IgM), 05% (NS1 + IgG) and 4% (NS1 + IgM + IgG) showed seropositivity.



**Fig. 5: ELISA- Pattern of Seropositivity**

### Discussion

Dengue fever is an acute infectious disease which presents with nonspecific fever that mimics many other viral illnesses. In India dengue is prevalent since last two centuries and first evidence of occurrence is from Vellore district in Tamil Nadu during 1956. In last decade, major outbreaks and deaths have occurred in Southern India (Andhra Pradesh, Tamil Nadu and Karnataka).<sup>8</sup>

In the present study slight male preponderance was seen that is, 59 % of patients were males and 41 % were females. The male to female ratio is found to be 1.43:1, which correlates with the study conducted by Kauser MM et al., (1.7:1).<sup>8</sup>

In this study most of the patients (56.7%) were aged less than 30 years, followed by 30 to 50 years (35.3%) and 50 to 75 years (08%). Similar findings were observed by Prakash B et al., as maximum number of patients occurred in age group 15-30 years (60%).<sup>4</sup>

In the present study dengue cases were found to be more during monsoon season. Similar pattern is reported by Kauser MM et al., The reason may be due to prime occupation of the people being agriculture and breeding of *Aedes aegypti* is highest during pre and post monsoon period.<sup>8</sup>

The common presenting symptoms include high-degree fever (100%), headache (70%), joint pains (45%), and skin rash (02%). Our clinical findings correlates with Prakash B et al., and Mohan K et al.<sup>4,5</sup> Retro-orbital pain was observed in 12% patients whereas Kauser MM et al., reported 12.32% patients. Bleeding manifestations were revealed in 8% of patients while Kauser MM et al., reported in 9.58%.<sup>8</sup>

Our study shows hypotension (7.33%) as a significant complication, followed by pleural effusion (5.33%). A similar study conducted by Kauser MM et al., shows pleural effusion (13.69%) as significant complication.<sup>8</sup>

Though dengue infection can be self-limiting with a milder clinical course, a small proportion may

progress to severe disease, characterized by plasma leakage, hemoconcentration, hemorrhagic shock and multiple organ failure leading to patient death.<sup>5,9</sup>

Thus a wide spectrum of clinical presentation with unpredictable clinical evolution and outcome warrants a diagnosis based on the clinical features supported by laboratory tests including non-specific haematological parameters and specific tests.

In our study total 77.2% of cases showed Thrombocytopenia as a common haematological abnormality out of which 45.3% showed (platelet count 50000-100,000/cu.mm), 21.3% (platelet count 20000-50,000/cu.mm) and 10.6% (platelet count < 20000/cu.mm). It may be due to either immune-mediated clearance of platelets or depressed platelet synthesis because of dengue virus induced bone marrow suppression. This correlates with studies of Kulkarni RD et al.,<sup>6</sup> and Jyothi P et al.,<sup>7</sup>

The laboratory investigations evaluated in our study showed that anaemia was observed in 6% of patients. Increased hematocrit was observed in 62% of patients. Leukopenia was observed in 53.3% of patients and was mainly found in NS1 seropositive patients. A similar study was conducted by Kauser MM et al., shows alike results.<sup>8</sup>

The diagnostic methods currently available for dengue diagnosis include viral culture, viral RNA detection by reverse transcriptase polymerase chain reaction and detection of dengue virus antigens or specific antibodies raised to them.<sup>3</sup>

In our study 70% samples showed NS1 antigen seropositive, 7% showed IgM antibody seropositive, 3% showed IgG seropositive whereas 20% showed more than one marker seropositive. In more than one markers seropositive samples, 11% (NS1 + IgM), 05% (NS1 + IgG) and 4% (NS1 + IgM + IgG) showed seropositivity. This correlates with studies of Kauser MM et al.,<sup>8</sup> and Anuradha M et al.<sup>10</sup>

The dengue virus contains single-strand RNA as genome. The genome is composed of three structural protein genes and seven non-structural protein (NS) genes. Among non-structural proteins, envelope glycoprotein, NS1 is essential for replication and viability of the virus. NS1 antigen appears as early as Day1 after the onset of the fever and declines to undetectable levels by 5–6 days. Hence detection of this antigen can be used for early diagnosis.<sup>11,12</sup>

Antibody response to infection comprises the appearance of IgM and IgG immunoglobulin isotypes, which are of diagnostic value in dengue. The titre of the IgM response is typically higher and more specific during a primary dengue infection when compared to secondary infections while the titre of the IgG response is higher during secondary infection than during primary infection.<sup>11,12</sup>

Primary dengue virus infection is characterized by elevations in specific IgM antibody levels 3 to 5 days after the onset of symptoms. IgG levels become

elevated after 10 to 14 days and remain detectable for life. During secondary infection, IgM levels generally rise more slowly and reach lower levels than in primary infection, while IgG levels rise rapidly from 1 to 2 days after the onset of symptoms.<sup>1</sup>

## Conclusion

Clinical suspicion and laboratory tests are needed to provide an early and accurate diagnosis of dengue virus infection for appropriate early patient management, to prevent development of complications like DHF and DSS and to initiate early public health control of dengue outbreaks.

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**How to cite this article:** Girish BRJ, Madhuri KR. A Clinico-microbiological study of dengue fever cases at Sri Siddhartha Medical College & Hospital, Tumkur. *Indian J Microbiol Res* 2016;3(2):209-212.