

# A study of clinical profile of patients with dengue fever with thrombocytopenia

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## Abstract

This study was done on 68 patients of dengue fever who were admitted in Bharati Hospital, Sangli during the period Jan. 2012 to Dec. 2013. All the patients require hospitalization due to one or the other complications of dengue fever like bleeding manifestations, shock, organ dysfunction etc. 57 patients recovered completely without any complications. While 11 patients expired due to severe dengue in spite of intensive management. These patients suffered from dengue haemorrhagic fever and dengue shock syndrome. It was observed that mortality was mainly due to plasma leak leading to shock, severe haemorrhage and multiorgan failure. Platelet count was not found to be a predictor of severity of disease or outcome. Effective fluid resuscitation by colloids, crystalloids and blood

**Keywords:** Dengue fever, Dengue Haemorrhagic fever, Dengue Shock Syndrome.

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## INTRODUCTION

Dengue is a self limiting acute mosquito transmitted disease characterized by fever, headache, muscle, joint pains, rash, nausea and vomiting. Dengue Fever (DF) is caused by an arbovirus and spread by Aedes mosquitoes. Some infections result in Dengue Haemorrhagic Fever (DHF) and in its severe form Dengue Shock Syndrome (DSS) can threaten the patient's life primarily through increased vascular Permeability and shock. The global prevalence has grown dramatically<sup>1</sup> in the recent decades. The WHO estimates that 40% of the world's population (about 2.5 billion) living in the tropical and sub tropical areas are at risk. Human population growth, unplanned urbanization, inadequate waste management and

international travel have led to spread of dengue fever to newer geographic areas. Since Aedes Aegypti breeding is more common in urban areas, the disease was prevalent in urban areas. However, the trend is now changing due to socio economic and manmade ecological changes leading to spread of dengue in rural areas. For a disease that is complex in its manifestations, management is relatively simple, inexpensive and very effective in saving lives A well managed front line response not only reduces the number of unnecessary hospital admissions but also saves the lives of dengue patients.

**Purpose Of the study:** Incidence of Dengue is Maximum in Maharashtra. Ours is a tertiary institute with maximum referral of all dengue patients in district. Common man and even general practioners have misconception about the management and outcome of disease. There is lack of knowledge about protocols about treatment of dengue and its complications.

## MATERIALS AND METHODS

This study was concluding in sixty eight patients with serologically confirmed dengue infection in Bharati Vidyapeeth Deemed University Medical College and Hospital, Sangli. Study period was one year (01 Jan 2012 to 31 Dec 2012). The sera was tested in the Department of Microbiology for IgM anti – dengue antibodies using

MAC-ELISA test according to NVBDCP guidelines for diagnosis of dengue. Patients were selected on basis of inclusion and exclusion criteria in study period. Data collected included the demographic details, details of clinical examination, and various laboratory parameters of blood counts, coagulation profile and biochemical investigation such as renal and hepatic function tests, treatment given, platelet transfusion and outcome of patient. Statistical analysis of data was done. The Chi Square test was used for analysis of the variables. A value of  $P < 0.05$  was considered significant.

### OBSERVATION AND RESULTS

The study included sixty eight patients with serologically confirmed dengue infection who required hospital admission in Bharati Vidyapeeth Deemed University Medical College and Hospital during the study period of one year. Demographic variables of study population. The study group consisted of 40 (58.82%) males and 28 (41.18%) females, with age ranging from 12-75 years with mean age of 35.6 years.

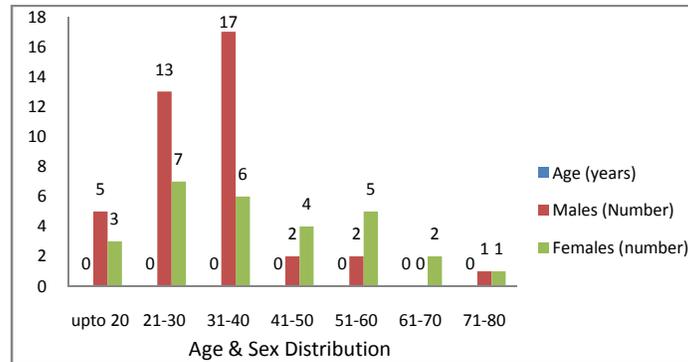


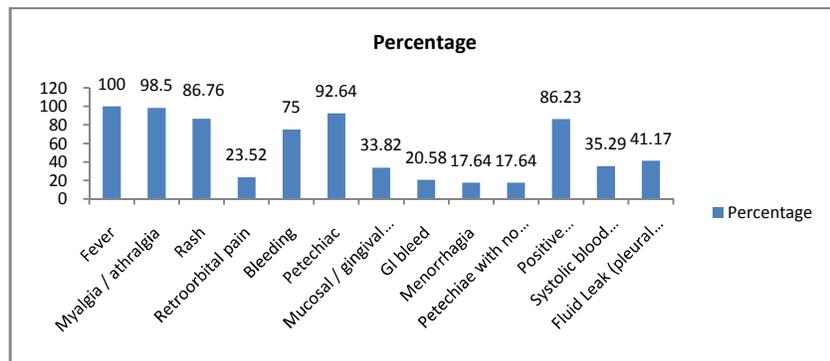
Figure 1: Age and sex wise distribution of Patients

No specific age predilection for the disease.

### CLINICAL PROFILE

Fever was the most common clinical presentation occurring in all the patients. Common clinical features seen in the study group were,

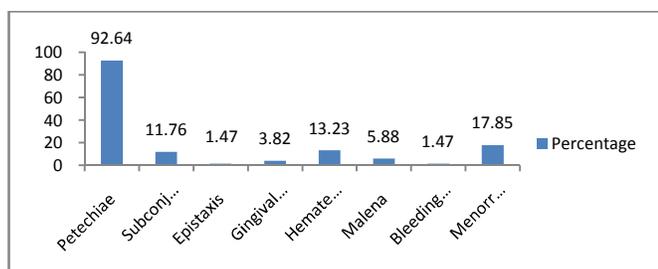
Fever- 100%, Athralgia and myalgia – 98.5%, Rash – 86.76%, Petechiac – 92.64%, Bleeding manifestations – 75%



Clinical features of patients with Dengue Fever, Myalgia and petechiae were most common presentations of patients under study.

### Bleeding Manifestations Seen In Patients Under Study

- Hemorrhagic manifestation
- Of the 68 patients, 63 (92.64%) had petechiae at presentation and 51 patients had clinical bleeding.
- 19 patients presented with major hemorrhagic manifestations (hematemesis, malena, bleeding PR, menorrhagia) whereas, twelve patients received platelet transfusion, due to clinical bleeding manifestation.



**Table 1: Thrombocytopenia profile**

Platelet Count	No. of cases	Percentage (%)
Platelet count > 1 lakh	1	1.47
Platelet count 50,000, 1,00,000	18	26.47
Platelet count 20,000-49,000	48	20.58
Platelet count < 20,000	1	1.47

The most common finding was thrombocytopenia in 50 patients (71.43%) of the study group, had a platelet count less than 50,000/ $\mu$ l at presentation to hospital. The mean platelet count at admission was 46,0

### Shock

- Shock was seen in 24 patients (35.29%) of the patients, 11 (16.17%) had compensated shock (systolic blood pressure maintain but signs of reduced perfusion present) and 13 (19.11%) presents with hypotensive shock (systolic BP < 90 mmHg).
- Eleven patients with shock succumbed to the disease. Among the 11 patients with compensated shock, there were 4 deaths and 7 patients recovered. In those with hypotensive shock, there were 7 deaths and 6 patients improved.
- Analysis of the above data using the Chi-square test (P value of 0.000) revealed a significant association of shock with mortality.

**Table 2: Comparison of Mortality with shock**

		Outcome		Total
		Expired	Improved	
Shock	Absent	0	44	44
	Present	11	13	24
	<b>Total</b>	<b>11</b>	<b>57</b>	<b>68</b>

12 patients with major bleeding manifestations were in shock at the time of presentation. Using the Chi-square test, a P value of 0.007 was obtained which was statistically significant. Indicating that, the presence of shock was an important factor contributing to hemorrhage in DHF

- Twenty eight patients of the study population received platelet transfusion for hemorrhagic manifestations.
- Twenty one of these patients improved and seven died.
- There was no difference seen in the overall outcome in patients who were transfused with platelets and those who did not receive any platelet transfusion. A p value of 0.187 was obtained using the Chi square test which was not statistically significant.

### DISCUSSION

Dengue infection has a wide clinical spectrum which includes both severe and non severe clinical manifestations. However simple but effective triage principles and management decisions at primary and secondary care levels can identify those at risk of developing severe disease and needing hospital care(9) In the present study 68 patients of dengue infection requiring hospital admission due to hypotension, bleeding manifestations, evidence of fluid leak, organ impairment, pregnancy, or other co morbid conditions were included. The study included 68 patients with forty (58.82%) male and twenty eight (41.17%) female patients. The ages of the patients ranged from 12 to 75 years. Several studies in Southeast Asia and Latin America have reported a higher association of DHF with older ages. Surveillance data also showed a shift in peak dengue mortality from pediatric ages to adults. Majority of the patients (64.2%) in this study were in the economically productive age group of 21-40 years, contributing significantly to the economic burden of the disease. The most common clinical features were fever (100%), athralgia and myalgia (98.53%), rash (86.76%), petechiae (92.65%), bleeding manifestations (75%). Hemorrhagic manifestations were seen in fifty one patients, of which nineteen patients had major bleeding manifestations (hematemesis, malena, bleeding per rectum, hemoperitoneum) and the rest had minor bleeding manifestations (ecchymosis, purpura, subconjunctival hemorrhage). Twelve patients had only petechiae but no other bleeding manifestations. Thrombocytopenia is the most common hematological finding in patients with dengue infection. Thrombocytopenia is caused due to IgM antiplatelet antibodies which induce platelet lysis via complement activation<sup>11</sup> and also inhibit ADP induced platelet

aggregation. 50 patients in this study had a platelet count of less than 50,000/uL at presentation. The mean platelet count at admission was 46,085/uL. None of the patients with severe hemorrhage had platelet counts <20,000/uL; 16 patients with severe bleeding had counts between 20,000-49,000/uL and four of these patients had a platelet count of > 50,000/uL. This shows that the platelet count does not correlate with the severity of bleeding. The role of platelet transfusion in DHF/DSS remained controversial. *Lye et al*<sup>13</sup> in their study observed that thrombocytopenia did not correlate with bleeding risk and the efficacy of prophylactic platelet transfusion is questionable. *Lum et al*<sup>14</sup> noted that in pediatrics DSS prophylactic transfusion of platelets and FFPs did not reduce bleeding or expedite platelet recovery, instead it caused fluid overload and prolonged hospitalization. *The WHO guidelines state that "prophylactic platelet transfusion for severe thrombocytopenia in otherwise hemodynamically stable patients have not been shown to be effective and are not necessary"* (10) *Ahluwalia et al*<sup>(16)</sup> suggest that "since there is no other specific therapy for DHF/DSS, patients with bleeding tendency and/or a platelet count less than 25000 may be transfused platelets." Twenty eight patients in this study received platelet transfusion, of these 12 patients had severe bleeding manifestations. In the group of patients received platelet transfusion there were 7 deaths and 21 patients improved. On statistical analysis there was no significant difference in outcome, seen in those who received and those who did not receive platelets (p=0.129). Hemorrhage is one of the major manifestations of DHF/DSS. Although severe bleeding occurs in DHF/DSS, it is multifactorial and not caused by thrombocytopenia alone. *Lum et al* in their study identified duration of shock and a low-normal hematocrit at the diagnosis of shock, as the strongest risk factors for hemorrhage. Massive bleeding can also occur in the absence of prolonged shock when aspirin, NSAIDs or corticosteroids have been taken.<sup>10</sup> Following the febrile (viremic) phase, the patient may either recover or progress to the leakage phase, leading to dengue hemorrhagic fever or dengue shock syndrome. Peak plasma viremia and circulating levels of the dengue virus nonstructural protein NS1, correlate with the severity of dengue infections. The increased number of infected cells results in increased production of cytokines, including TNF- $\alpha$  and IFN- $\alpha$ , and other chemical mediators and is responsible for increased vascular permeability, abnormal leakage of plasma, hypovolemia, shock, and hemostatic abnormalities. A similar association was seen in this study. Nineteen patients in the study group had severe hemorrhage. In 60% of these patients severe hemorrhage was associated with shock and 40% had severe bleeding

in the absence of shock. On statistical analysis of data it was seen that there was a significant association between shock and the presence of severe bleeding (p value =0.004) in the patients studied. Shock occurs when a critical volume of plasma is lost through leakage. During the initial stages of shock, compensatory mechanisms maintain a normal systolic blood pressure, producing tachycardia and peripheral vasoconstriction (*compensated shock*).<sup>(10)</sup> There is rise of diastolic blood pressure towards systolic blood pressure leading to a narrow pulse pressure. Finally there is decompensation and both pressures disappear (*hypotensive shock*). Twenty four (35.29%) patients in the study group presented with shock. Eleven patients had compensated shock (maintained systolic BP with signs of reduced perfusion) and thirteen had hypotensive shock. The mortality among the patients with shock was 45.8% i.e. eleven patients with shock succumbed to the disease. The latest WHO guidelines<sup>5</sup> emphasize that judicious intravenous fluid resuscitation is essential and usually the sole intervention required. The guidelines state that there is no clear advantage of colloid over crystalloid fluids in terms of overall outcome. However, colloids may be the preferred choice if blood pressure has to be restored urgently (<10 mm of Hg)<sup>10</sup>. *Premratna et al*<sup>7</sup> suggest that during the resuscitation of patients who already have evidence of third space fluid accumulation at the time of developing DSS, use of colloids rather than crystalloids would prevent the development of recovery phase pulmonary edema. *Wills et al*<sup>8</sup> in their double blind randomized comparison of fluid for initial resuscitation of children with DSS concluded that resuscitation with crystalloids was acceptable for children with moderately severe DSS. In this study group all patients received crystalloid solution for fluid resuscitation. Patients with profound shock and coagulopathy received fresh frozen plasma and blood. The assessment of the efficacy of colloid solutions versus crystalloids in the resuscitation of patients with shock was limited by the unavailability of colloid solutions such as dextrans, starch, gelatin etc. There was a mortality of 15.7% in the patients studied. Eleven of sixty eight patients succumbed to the disease, of these there were ten male and only one female death. There was no specific association of mortality with any particular age group in the study population. Prolonged shock is a major factor contributing to death as it leads to hypoxia, organ dysfunction, DIC and severe hemorrhage. Seven patients who succumbed to dengue had severe bleeding manifestations (hematemesis, massive bleeding PR, hemoperitoneum), two patients had minor bleeding (subconjunctival hemorrhage, oral bleeding), two patients only had petechiae with no other bleeding manifestation.

## CONCLUSION

From this study it was concluded that:

- The main factor contributing to the mortality was the presence of shock which lead to severe hemorrhage and organ dysfunction.
- The main focus in the management of dengue should be on preventing the development of shock and rapid correction of shock with careful i.v. fluid administration. The key is to maintain the blood pressure to prevent tissue hypoxia and organ dysfunction.
- Platelet count does not correlate with severity of hemorrhage or mortality.
- Platelet transfusions may be of benefit in patients with thrombocytopenia and hemorrhage, which continues despite blood transfusion.

## LIMITATIONS

In this study it was not possible to determine whether the dengue infection in the patients studied was a primary or a secondary infection. Therefore, we were unable to evaluate whether development of severe dengue and mortality was more in patients with primary or secondary dengue infections. The tests for virus isolation, antigen detection and identification of the infecting serotype are not available in our hospital. The results of the MAC ELISA test are not available immediately therefore confirmation of diagnosis is delayed. We could not compare the effectiveness of various IV fluids (crystalloids v/s colloids) used for initial resuscitation as most of our patients received crystalloids.

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