

## Original Research

### Evaluation of Dengue Fever with Thrombocytopenia and associated complications

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#### ABSTRACT:

**Background:** Dengue is one of the most prevalent mosquito-borne arboviral infection in India. It is characterized by leucopenia followed by thrombocytopenia. In general, dengue is a self-limiting acute febrile illness followed by a phase of critical defervescence, in which patients may improve or progress to a severe form. Severe illness is characterized by hemodynamic disturbances, increased vascular permeability, hypovolemia, hypotension, and shock. **Materials and methods:** Data were collected from patients attending outpatient and inpatient services in a hospital in North India. Total 58 patients of both sexes with age 35±10 years admitted with fever and found to have thrombocytopenia are included in the study. Data were collected after obtaining consent in due format. Data are collected by using interview, physical examination, sputum examination, and laboratory findings. **Result:** Out of 116 cases with severe thrombocytopenia, complications were present in 72 cases. Thirty eight patients had haemorrhagic dengue fever, 10 suffer from severe dehydration, 6 from DHF with bleeding manifestation, 6 from dengue shock syndrome, 4 from fever induced seizures, 8 from neurological complications. **Conclusion:** It one of the most common vector-borne diseases worldwide. thrombocytopenia can be used as predictor of complications in a patient with dengue fever. So both Clinical as well as laboratory monitoring of Dengue patients for hemorrhagic manifestations and marked thrombocytopenia is strongly recommended.

**Key words:** Dengue, thrombocytopenia, Fever, Platelet count, Dengue Shock syndrome (DSS).

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#### INTRODUCTION:

Dengue is one of the most prevalent mosquito-borne arboviral infection in India. Seventy percent of the 96 million apparent infections occur in Asia, in which India is making upto one third of the total. Despite considerable efforts to control the mosquito populations, dengue fever has emerged, spread and established itself rapidly. The most serious manifestations of the infection are Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS).<sup>1-4</sup>

Human transmission of dengue is also known to occur after occupational exposure in health care settings (e.g., needle stick injuries) and cases of vertical transmission have been described in the literature (i.e., transmission from a dengue

infected pregnant mother to her fetus in utero or to her infant during labor and delivery).<sup>5-8</sup>

Thrombocytopenia and platelet dysfunction are common in both cases and are related to the clinical outcome.<sup>9</sup> Different mechanisms have been hypothesized to explain DENV-associated thrombocytopenia, including the suppression of bone marrow and the peripheral destruction of platelets.<sup>10</sup> Thrombocytopenia may be associated with alterations in megakaryocytopoieses by the infection of human hematopoietic cells and impaired progenitor cell growth, resulting in platelet dysfunction (platelet activation and aggregation), increased destruction or consumption (peripheral sequestration and consumption).<sup>11</sup> Hemorrhage may be a consequence of the thrombocytopenia and

associated platelet dysfunction or disseminated intravascular coagulation.<sup>12</sup> During first 3 days of illness platelet count is normal, thrombocytopenia begins during febrile phase and platelet count is progressively reduced during hemorrhagic illness (DHF). As per WHO guidelines, thrombocytopenia can be used as simple diagnostic criteria for DHF which is roughly estimated by microscopy even in the peripheral laboratories [9, 10]. Spontaneous bleeding is noted platelet count of <20,000 which signifies the need to evaluate platelet count and follow up after platelet transfusion thereby curtailing further progression of disease to its severe forms and thus increasing positive prognosis

**MATERIALS AND METHOD:**

The present study was a retrospective study conducted on total 116 patients with mean age 32.6 years admitted with fever and found to have thrombocytopenia are included in the study. Out of 116 patients 70 were males and 46 were females. Data were collected after obtaining consent in due format. A brief history taking was done including age, weight, any medical condition. Physical examination, sputum examination, and laboratory data were obtained by trained physicians. Evaluation of Blood samples collected

from all patients with NS 1 Antigen, IgM, IgG antibodies positivity experiencing febrile illness, clinically consistent with dengue infection was done in all these cases. Laboratory tests including hematocrit and platelets counts were registered. The association between severe thrombocytopenia and the presence of complications were evaluated. Samples were examined within 5 hours of the initial sample collection and Platelet counts were calculated in patients who were found seropositive for dengue infection. Mean platelet count, number of complications, WBC count and duration of hospital stay were evaluated and follow up was done.

**RESULTS:**

A total of 116 patients were diagnosed with dengue fever based on laboratory findings. Amongst them 70 were males and 46 were females. The mean age obtained was 32.6 years. Out of total number of cases with severe thrombocytopenia, complications were present in 72 cases; 38 patients had haemorrhagic dengue fever, 8 were having neurological complications, 10 suffer from severe dehydration, 6 from DHF with bleeding manifestation, 6 from dengue shock syndrome and 4 from fever induced seizures.

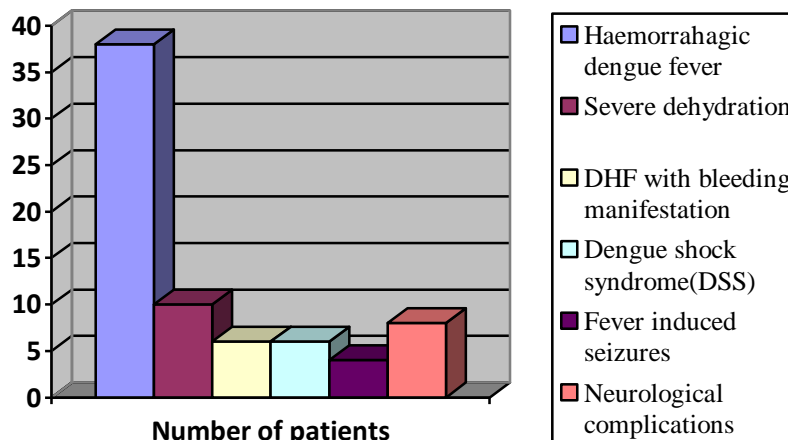
**Table 1:** Distribution of sex

Gender	Number of cases(n=116)
Males	70
Females	46

**Table 2:** Demographic variables in patients having dengue fever

Variables	Value
Mean age	32.6 years
Mean platelet count	0.75 lakhs/mm <sup>3</sup>
Having leucopenia	36
Average duration of hospital stay	6.2 days

**Graph 1:** Complications in hospitalized patients



Various nonhemorrhagic and neurological complications were known to occur in patients having dengue with thrombocytopenia. These includes hepatitis, transaminitis, acute kidney injury, acute respiratory distress syndrome (ARDS) and meningoencephalitis.

The mean platelet count was 0.75 lakhs/mm<sup>3</sup>. The relation between platelet count and number of complications was studied. There was a negative correlation between platelet count and complications rate. This indicates that lower the platelet count more are the complications.

In our study, 36 patients had leucopenia (31.03%). The relationship between leucopenia and platelet count was studied. Leukopenia with thrombocytopenia showed a positive correlation but was not statistically significant. This suggests that platelet count may not have any relation with leukocyte count.

The average duration of hospital stay was 6.2 days. There was a negative correlation between platelet count and duration of hospital stay and it was statistically significant. This suggests that as platelet count decreases the duration of hospital stay increases. The possible explanation could be that as per above correlation number of complications is increasing with lower platelet count, hence increased duration of hospital stay.

#### **DISCUSSION:**

Dengue causes serious infection in humans, resulting in morbidity and mortality in most tropical and subtropical areas of the world. It is estimated that there are currently 50–100 million cases of dengue every year worldwide, including more than 500,000 reported cases of dengue hemorrhagic fever and dengue shock syndrome (DHF/DSS)<sup>15</sup>. Thrombocytopenia has always been one of the criteria used by WHO guidelines as a potential indicator of clinical severity<sup>16</sup>. In the most recent 2009 WHO guidelines, the definitions generally describe a rapid decline in platelet count or a platelet count less than 150,000 per microliter of blood.<sup>16</sup> A kinetic description of platelet count in DHF/DF showed a significant decrease on the 4th day of the illness.<sup>17</sup>

Dengue fever (DF) with its severe manifestations such as dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) has emerged as a major public health problem of international concern.<sup>18</sup> Leukopenia was observed in 31.03% in present study. Neutropenia may be due to marked degeneration of mature neutrophils and “shift to left during febrile phases of illness. A study by Ahmed et al, leukopenia was observed in 43%.<sup>19</sup> A study by Dhooria et al, hepatic dysfunction was seen in 14.8%, leukopenia in 26% cases and two patients in his study had organ impairment.<sup>20</sup> Prathyusha et al, in her study at eluru showed that with increasing severity of leukopenia there is increased the incidence of hemorrhagic manifestations (P value 0.023).<sup>21</sup> However, she found no significant association of leukopenia with significant bleeding manifestations. Relationship between platelet count and

bleeding manifestations has been extensively evaluated. Raikar *et al.* showed in his study that bleeding manifestations are not related to platelet count.<sup>22</sup> The relationship between platelet count and non-hemorrhagic complications is less studied.<sup>22</sup>

It has been suggested that thrombocytopenia arises from both decreased production of cells from bone marrow associated with an increased peripheral destruction of platelets.<sup>24</sup> Several mechanisms are involved in thrombocytopenia and platelet dysfunction in dengue, indicating the complexity of dengue immunopathogenesis.<sup>25,26</sup> Patient with lower platelet count was found to have higher chances of developing complications.<sup>27</sup> In our study, there is with positive correlation between platelet count and complications. As the platelet counts decreased, complications risk increased in the clinical outcome of dengue fever.

Redkar et al aimed to study the clinical profile of patients presenting Dengue fever with thrombocytopenia & to study the outcome of patients with respect to severity of thrombocytopenia in Dengue fever and associated co morbid medical conditions. They observed that out of enrolled 127 patients 89(70.08%) patients were male and 38 (29.92%) were females. Mean age of presentation was 26.20 ± 10.92 years. Bleeding Tendency was present in 26 (20.47%) patients. Other complication like Hepatic failure in 7 (5.51 %) patients, Renal failure in 12 (9.44 %) patients, acute respiratory distress syndrome (ARDS) in 9 (7.08%) of patients & Multi Organ Dysfunction Syndrome (MODS) was observed in 7 (5.51 %) patients. Overall 7 (5.51%) patients died during ward stay of which MODS with disseminated intravascular coagulation (DIC) (71%) was the commonest cause of death followed by ARDS. Authors concluded that severe thrombocytopenia was found to be associated with shock, bleeding tendency, anaemia, renal failure, severe hepatic involvement and ARDS to a significant extent.<sup>28</sup>

The lack of correlation between low platelet counts and bleeding manifestations has been noted in dengue patients when compared to the previous studies. However, there was statistically significant difference in severe thrombocytopenia with complications, which is contrary to previous studies.

#### **CONCLUSION:**

Platelet count can be used to predict complication rate in a patient admitted with dengue fever. Though leukopenia is seen early in the disease there is no significant correlation to complication rate. Severe thrombocytopenia was found to be associated with shock, bleeding tendency, anaemia, renal failure, severe hepatic involvement and ARDS to a significant extent and low haemoglobin, higher total leucocyte count, severe hepatitis, renal failure, and coagulopathy were significantly associated with mortality. So, thrombocytopenia can be used as predictor of complications in a patient with dengue fever. So both

Clinical as well as laboratory monitoring of Dengue patients for hemorrhagic manifestations and marked thrombocytopenia is strongly recommended.

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