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ORIGINAL ARTICLE

DENGUE FEVER WITH THROMBOCYTOPENIA AND IT'S COMPLICATIONS: A HOSPITAL BASED STUDY

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ABSTRACT:

Background: Dengue fever is a disease spread by the Aedes aegypti mosquito and is caused by one of four dengue viruses. This mosquito is a tropical and subtropical species widely distributed around the world. Dengue 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 58 cases with severe thrombocytopenia, complications were present in 36 cases.19 patients had haemorrhagic dengue fever, 5 suffer from severe dehydration, 3 from DHF with bleeding manifestation, 3 from dengue shock syndrome, 2 from fever induced seizures, 4 from neurological complications. **Conclusion**: It one of the most common vector-borne diseases worldwide.There was no predilection for any age group or gender for thrombocytopenia or bleeding among the dengue patients.

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

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INTRODUCTION:

Dengue fever is a disease spread by the Aedes aegypti mosquito and is caused by one of four dengue viruses.[1] Once you are infected with one of the dengue viruses, you will develop immunity to that virus for the rest of your life. However, you can still be infected with the other three viruses. It is possible to get all four dengue viruses in your lifetime. The viruses that cause dengue fever are related to those that cause yellow fever and West Nile virus infection.[2]The mosquito becomes infected when it bites a person with dengue virus in their blood. It can't be spread directly from one person to another person.

Symptoms, which usually begin four to six days after infection and last for up to 10 days, may include: sudden high fever, severe headaches, pain behind the eyes, severe joint and muscle pain, fatigue, nausea, vomiting, skin rash, which appears two to five days after the onset of fever, mild bleeding (such a nose bleed, bleeding gums, or easy bruising).[3,4] Sometimes, symptoms are mild and can be mistaken for those of the flu or another viral infection. Younger children and people who have never had the infection before tend to have milder cases than older children and adults. However, serious problems can develop. These include dengue hemorrhagic fever, a rare complication characterized by high fever, damage to lymph and blood vessels, bleeding from the nose and gums, enlargement of the liver, and failure of the circulatory system.[5] The symptoms may progress to massive bleeding, shock, and death. This is called dengue shock syndrome (DSS). Symptoms of shock includes a sudden drop in blood pressure; cold, clammy skin, a weak rapid pulse, dry mouth, irregular breathing, dilated pupils, reduced flow of urine.[6,7] Mortality rates can be as high as 40% if this serious complication is not treated. If it is treated, the mortality rate is 1-2%.[8]

Thrombocytopenia and platelet dysfunction are common in both cases and are related to the clinical outcome. [9] Different mechanisms have been hypothesized to explain DENV-associated thrombocytopenia, including the suppression of bone marrow and the peripheral destruction

of platelets.[10] 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).[11] Hemorrhage may be a consequence of the thrombocytopenia and associated platelet dysfunction or disseminated intravascular coagulation.[12]

The disease progresses in three phases - febrile phase, critical phase and recovery phase. Complications develop during the critical phase.

MATERIALS AND METHOD:

This study was conducted in hospital, in North India. Total 58 patients with age 35±10 years admitted with fever and found to have thrombocytopenia are included in the study. Out of 58 patients 35 were males and 23 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.

RESULT:

A total of 58 patients were diagnosed with dengue fever based on labortary findings. Amongst them 35 were males and 23 were females. The mean age obtained was 28.6 years. Out of total number of cases with severe thrombocytopenia, complications were present in 36 cases; 19 patients had haemorrhagic dengue fever, 4 were having neurological complications, 5 suffer from severe dehydration, 3 from DHF with bleeding manifestation, 3 from dengue shock syndrome and 2 from fever induced seizures.

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 0.77 lakhs/mm^3. 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, 18 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 4.1 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.

Graph 1: Distribution of sex

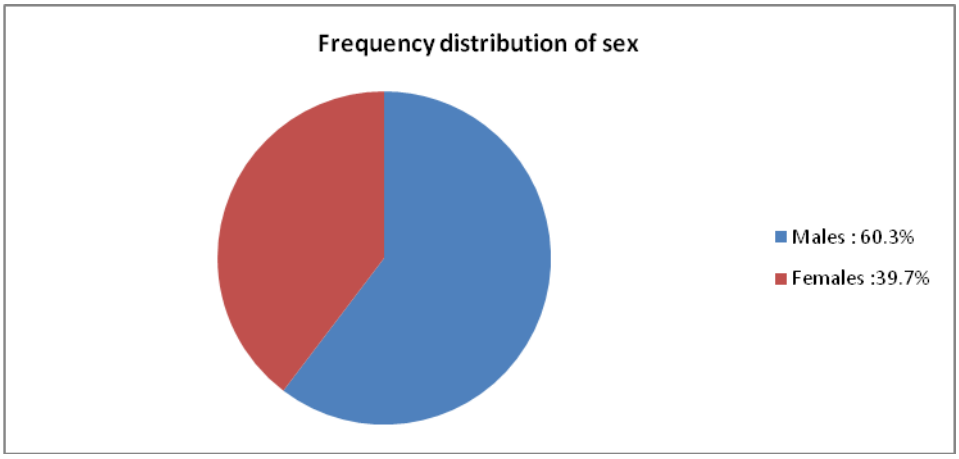

Table 1: Demographic variables in patients having dengue fever

Variables	Value
Mean age	28.6 years
Mean platelet count	0.77 lakhs/mm^3
Having leucopenia	18
Average duration of hospital stay	4.1 days

Table 2: Complications in hospitalized patients

Complications	Number of patients
Haemorrahagic dengue fever	19 (32.7%)
Severe dehydration	5 (8.62%)
DHF with bleeding manifestation	3 (5.17%)
Dengue shock syndrome(DSS)	3 (5.17%)
Fever induced seizures	2 (3.44%)
Neurological complications	4 (6.89%)

DISCUSSION:

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.[13] Severe illness is characterized by hemodynamic disturbances, increased vascular permeability, hypovolemia, hypotension, and shock. Thrombocytopenia and platelet dysfunction are common in both cases and are related to the clinical outcome.[14] 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) [15]. Thrombocytopenia has always been one of the criteria used by WHO guidelines as a potential indicator of clinical severity [16]. 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.[16] A kinetic description of platelet count in DHF/DF showed a significant decrease on the 4th day of the illness.[17]

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. [18] 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%.[19] A study by Dhooria et al, hepatic dysfunction was seen in 14.8%, leucopenia in 26% cases and two patients in his study had organ impairment.[20] 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).[21] 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.[22] The relationship between platelet count and nonhemorrhagic complications is less studied.[23]

It has been suggested that thrombocytopenia arises from both decreased production of cells from bone marrow associated with an increased peripheral destruction of platelets.[24] Several mechanisms are involved in thrombocytopenia and platelet dysfunction in dengue, indicating the complexity of dengue immunopathogenesis.[25,26] Patient with lower platelet count was found to have higher chances of developing complications.[27] 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.

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. Our study showed no significant correlation between hemorrhagic and non-hemorrhagic manifestations with low platelet count which was existent in previous literature. In recent years, emphasis has been placed on community-based approaches to larval source reduction to provide program sustainability. Community participation in and ownership of prevention programs require extensive health education and community outreach. Unfortunately, this approach is a very slow process.

Precautions, therefore, include staying in screened or air-conditioned rooms, spraying these rooms with aerosol bomb insecticides to kill adult mosquitoes indoors (especially in bedrooms), using a repellent containing

dimethyl-metatoluamide (DEET) on exposed skin, and wearing protective clothing treated with a similar repellant.

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