

## Dengue: a clinical & hematological study

Evelyn Angel S<sup>1</sup>, Sivasankaran M<sup>2</sup>, Elizabeth Chacko<sup>3</sup>

<sup>1</sup>Dr. Evelyn Angel S, Assistant Professor, <sup>2</sup>Dr. Sivasankaran M, Professor, <sup>3</sup>Dr. Elizabeth Chacko, Professor and HOD, all authors are affiliated with Department of Pathology, Sree Mookambika Institute of Medical Sciences, Kulasekharam, Tamil Nadu, India.

**Address of Correspondence:** Dr. Evelyn Angel S, Assistant Professor, Department of Pathology, Sree Mookambika Institute of Medical Sciences, Kulasekharam, Tamil Nadu. Email id: evelynangel@rediffmail.com

### Abstracts

**Introduction:** Dengue has positioned itself as the most important mosquito borne viral disease in the world. Current estimates report that at least 112 countries are endemic for Dengue and around 40% of the world populations are at risk in tropics and subtropics. **Objective:** The objective of this study is to analyze the hematological findings in dengue illness and to correlate the same with the clinical course. **Materials and Methods:** The present study was conducted in the Department of Pathology, Sree Mookambika Institute of Medical Sciences, Kulasekharam, Kanyakumari District, Tamilnadu during a period of three years from 2013 to 2015, where fifty dengue positive cases were analyzed from the Department of General Medicine. **Results:** A history of fever with retroorbital pain, myalgia and headache was noted in 7 (14%), 43 (86%) and 50 (100%) of the cases respectively. Of the cases studied, only one (2%) of the patients had a major bleeding manifestation, whereas minor bleeding manifestations were noted in 8 (16%) of the cases. Thrombocytopenia was noted 48 patients. Leukopenia was observed in 22 (73%), while leukopenia with reversal of neutrophil lymphocyte ratio was observed in 6 (20%) of the patients. A rising haematocrit was noted in (16%) of the cases. **Conclusion:** It was concluded in this study that fever in the presence of thrombocytopenia, leukopenia, reversal of neutrophil lymphocyte ratio and a rising haematocrit should raise a strong suspicion of Dengue fever for which confirmation must be done. Thrombocytopenia was found to be an important prognostic indicator during hospital stay and/or follow up.

**Key words:** Dengue, clinical symptoms, thrombocytopenia, WBC counts.

### Introduction

The first reported epidemics of dengue illness occurred in 1779-1780 in Asia, Africa and North America. The near concurrent incidence of outbreak in three continents shows that these single stranded RNA viruses and their mosquito vectors have had a world wide circulation in the tropics for more than two hundred years [1,2].

A pandemic of dengue began in South East Asia after World War II and has spread around the world. Since then epidemics caused by multiple serotypes (Hyperendemicity) are more recurrent the geographic circulation of dengue viruses and their mosquito vectors has extended and DHF has emerged in the Americas and the Pacific region [1].

Haematological parameters like Hb level, total WBC count, differential WBC count and platelet count are altered in dengue fever. The most common findings are thrombocytopenia with concurrent haemoconcentration. A guide for analysis, treatment and containment of Dengue fever prepared by technical advisory committee on Dengue Haemorrhagic fever for South East Asia Western Pacific areas in 1975 & 1980 has been modified by WHO.[1] The criteria include 4 Major manifestations such as:

- I. Major manifestations of fever
- II. Haemorrhagic manifestations
- III. Hepatomegaly
- IV. Tendency to develop shock, two laboratory changes (i.e) thrombocytopenia and concurrent haemoconcentration which have been proven to be practical in 95% cases.

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Other important laboratory findings:

1. Leucopenia
2. Lymphocytosis with reactive Lymphocytes
3. Increased capillary permeability and presence of thrombocytopenia[3,4,5,6]
4. Elevated liver enzymes

Current estimates report that at least 112 countries are endemic for Dengue and around 40% of the world populations are at risk in tropics and subtropics. Annually around 100 million cases of dengue fever and half a million cases of DHF occurs worldwide[1,7]. Today Dengue has positioned itself as the most important mosquito borne viral disease in the world. This study was done to analyze the haematological findings in dengue illness and correlate the same with the clinical course and by doing so help in aiding the diagnosis of dengue and prevent mortalities related to this illness.

## Methods

**Study design:** Descriptive cross-sectional study

**Study settings:** The present study was conducted in the Department of Pathology, Sree Mookambika Institute of Medical Sciences, Kulasekharam, Kanyakumari District, Tamilnadu during a period of three years from 2013 to 2015. The study was approved and ethically cleared by the Institutional Human Ethics Committee (IHEC).

### Inclusion criteria

1. All serologically positive dengue patients (Dengue NS1 antigen, IgM antibody).
2. Age 13 years and above.

### Exclusion criteria

1. Suspected dengue cases in which serology is found to be negative.
2. Serologically positive cases of dengue who are also positive for other coexisting infections e.g. Malaria, typhoid.
3. Patients not giving consent.

**Participants:** In the present study fifty cases were taken from the Department of General Medicine, Sree Mookambika Institute of Medical Sciences, Kulasekharam. Fifty clinically suspected cases of dengue

above the age of 13 confirmed by serological studies of IgM ELISA with or without NS1 antigen positivity were taken and the various parameters were studied. They were followed from the day of admission to time of recovery or discharge.

**Variables:** Age, duration of fever, grade of thrombocytopenia, WBC count and distribution

**Data source:** Sree Mookambika Institute of Medical Sciences, Kulasekharam

**Bias:** Nil

**Data size:** 50

**Quantitative variables:** Grade of thrombocytopenia, WBC count and distribution

**Statistical methods:** The data was expressed in number and percentage (%). The percentage was calculated by using Microsoft excel (Windows 2007) software.

**Collection of Data:** Fifty clinically suspected cases of dengue were screened and their consent for the study obtained. Patients clinical data were collected from the medical records. Data was then collected in a predesigned questionnaire.

2-5ml of venous blood is collected in vacuum tubes or disinfected vials with screw caps and gasket. Adhesive tape marked with pencil, permanent ink or a type written/ printed self adhesive label to recognize the container.

The name of the patient, identification number and date of collection will be indicated on the label. Serological confirmation by dengue specific NS1 antigen assay and/or IgM by ELISA were done. Clinical parameters of each serologically dengue positive patient was recorded.

Haematological parameters like Haemoglobin, Packed cell volume, Total WBC count, Differential WBC count was done by automated cell counter and recorded. Platelet count was done by automated cell counter (Beckman Coulter Ac.T 5 Diff). If flagging occurred for the values manual count was done. Peripheral smears were made and stained with Leishman's stain and the report of the smear was recorded.

The data obtained was tabulated in the master chart with the various parameters to be observed and studied.

## Results

Out of fifty cases of serologically positive dengue cases studied 8(16%) cases were in the age group of 14-20 years, 13 (26%) were in the age group 21-30 years, 13(26%) were in the age group 31-40 years, 7(14%) were in the age group of 41-50 years, 3(6%) were in the age group of 51-60 years, 5(10%) were in the age group of 61-70 years and one (2%) case was above 70 years of age.

Out of the 50 cases studied 29(58%) were males and 21(42%) were females. In this study there was a slight male preponderance.

**Table-1: Distribution of patients according to age.**

Age (years)	Number	Percentage (%)
14-20	08	16.00
21-30	13	26.00
31-40	13	26.00
41-50	07	14.00
51-60	03	06.00
61-70	05	10.00
Above 70	01	02.00

Age group ranging from 21-40 showed the maximum distribution

**Table-2: Distribution of patients according to gender.**

Gender	Number	Percentage (%)
Male	29	58.00
Female	21	42.00

**Percentage of males was slightly higher than females**-Out of the fifty cases studied patients who had fever for 5 days duration were 13(26%), fever for 6 days were 17(34%), fever for 7 days were 12(24%), fever for 8 days were 3(6%), fever for 9 days were 1(2%) and fever for 10 days duration was 4(8%). 5-6 days was the most common fever duration in this study.

Out of the fifty cases studied 50(100%) of the patients had headache, 43(86%) had myalgia, 7(14%) had retroorbital pain, and 5(10%) had arthralgia. 6(12%) of the patients had upper respiratory tract infection, 8(16%) had lower respiratory tract infection. 14(28%) had abdominal pain, 20(40%) had vomiting, 26(52%) had hepatomegaly and 24(48%) had splenomegaly. Out of the fifty cases studied only one (2%) of the patients had major bleeding manifestation. 8(16%) of patients had minor bleeding manifestations and 41(82%) had no bleeding manifestation. 8(16%) had rising haematocrit.

**Table-3: Distribution of patients according to duration of fever.**

Duration of fever	Number	Percentage (%)
5 days	13	26.00
6 days	17	34.00
7 days	12	24.00
8 days	03	06.00
9 days	01	02.00
10 days	04	08.00

The maximum duration of fever noted was 6-7 days.

**Table-4: Distribution of patients according to musculoskeletal complaints.**

Musculoskeletal complaints	Number	Percentage (%)
Headache	50	100
Retro orbital pain	07	14.00
Myalgia	43	86.00
Arthralgia	05	10.00

Headache was seen in 100% of patients followed by myalgia.

**Table-5: Distribution of patients according to gastrointestinal complaints.**

Gastrointestinal complaints	Number	Percentage (%)
Abdominal pain	14	28.00
Vomiting	20	40.00

**Table-6: Distribution of patients according to hemorrhagic manifestation**

Hemorrhagic manifestation	Number	Percentage (%)
Major	1	02.00
Minor	8	16.00
Absent	41	82.00

16% showed minor bleeding manifestations like petichiae and bleeding gums

**Table-7: Distribution of patients according to signs of capillary leak**

Signs of capillary leak	Number	Percentage (%)
Pleural effusion	8	16.00
Ascites	13	26.00
Rise of hematocrit	8	16.00

Rise in haematocrit is seen in 16% of the patients, Ascites in 26%.

Out of the fifty cases studied 29(58%) showed positivity for IgM and 21(42%) showed positivity for NS1 and IgM. In the fifty patients studied 4(8%) had anemia, 3(6%) had leukopenia, 16(32%) had thrombocytopenia, 18(36%) had leukopenia with thrombocytopenia, 8(16%) had anemia with thrombocytopenia and 6(12%) of the patients had anemia with leukopenia and thrombocytopenia.

In the 50 patients studied 48 patients show thrombocytopenia. 12(25%) showed Grade 1 thrombocytopenia, 5(10.42%) Grade 2, 22(45.83%) Grade 3 and 9 (18.75%) Grade 4. In the fifty cases studied Leukopenia was observed in 22(73%) of the patients, Leukopenia with reversal of neutrophil lymphocyte ratio was observed in 6(20%) of the patients, 2(7%) had only reversal of neutrophil lymphocyte ratio.

**Table-8: Distribution of patients according to grade of thrombocytopenia.**

Grade of thrombocytopenia	Number	Percentage (%)
Grade-1 (75,000 to 1,50,000) cells/cu.mm	12	25.00
Grade-2 (50,000 to less than 75,000) cells/cu.mm	5	10.42
Grade-3 (25,000 to less than 50,000) cells/cu.mm	22	45.83
Grade-4 (less than 25,000) cells/cu.mm	9	18.75

Grade -3 was 45.83% of the total cases

**Table-9: Distribution of patients according to WBC count and distribution.**

WBC count and distribution	Number	Percentage (%)
Leukopenia (<4000 cells/cu.mm)	22	73.00
Leukopenia with reversal of neutrophil lymphocyte ratio	6	20.00
Reversal of neutrophil lymphocyte ratio	2	07.00

Leukopenia was seen in 93% of cases and 27% showed reversal of neutrophil lymphocyte ratio.

## Discussion

Dengue fever remains the most important of the arboviral infections with significant socioeconomic and healthcare implications. The clinical spectrum ranges from non-specific viral syndrome to classical dengue fever to life threatening dengue haemorrhagic fever and dengue shock syndrome. Early diagnosis and aggressive management especially for DHF and DSS remains the cornerstone strategy for successful outcomes.

**Clinical features and demography:** A total of 50 patients admitted to our hospital with symptoms of dengue fever and positive NS1 and/or IgM ELISA were studied [8,9,10,11,12]. The average age of patients in our study group was 36.84 years. In the study by Saquib MA et al. and Tiwari KN et al. similar observations were noted [13,14].

Out of the 50 cases included in our study 29 (58%) were males and 21 (42%) were females, similar in comparison to the study done by Saquib MA et. al and Raju BJ et.al [13,15].

All patients in our study presented with fever on admission. Similar observation were found in other studies [13-18]. Retroorbital pain is considered a hallmark of Dengue fever. The number of patients in our study manifesting this were 7 (14%) out of the 50 cases. Raju BJ et.al in their study of 200 dengue cases reported a 26.5% incidence of retroorbital pain [15]. Arthralgia was noted in 5 (10%) of the patients in our study. Raju BJ et.al reported an incidence of 16% among their study group [15].

Headache was present among all our patients (100%). In other studies, the incidence of headache was as follows, Raju BJ et. al (98%), Turbadkar D et.al (13.9%), Mandal KS et.al (62.16%), Lt .Col. Banerjee M et.al (63%), Khan AH et al (50%). [15,16,17,19,20]. Our study differed from most of the other studies as headache was not a prominent symptom in those studies.

Abdominal pain was another presenting complaint in 14 (24%) of our patients. Tiwari KN et.al and Raju BJ et.al noted slightly higher percentage in comparison to our study [14,15]. Nausea and vomiting was reported in 20 (40%) patients. Other authors reported slightly higher incidence [14,15,20].

Our study noted that 43 (86%) out of 50 patients had myalgia. Some authors showed similar observations [4,7,9]. Others were observed slightly lower percentage of myalgia [14,16,20].

Hepatomegaly was observed in 26 (52%) of our patients. Raju BJ et al and Banerjee M et.al reported a 30% and 15% incidence among their patients [4,9]. Splenomegaly was noted in 24 (48%) our patients. Banerjee M et.al reported splenomegaly in only 7% of the total patients [19].

We encountered URTI in 6 (12%) of our patients and 8 (16%) had lower respiratory tract infection. Khan AH et al reported 35% of cases with URTI in their study [20].

**Haematological parameters:** Our study revealed an incidence of anemia in 8% (4 patients) whereas the study conducted by Banerjee M et.al revealed an incidence of 11% in 50 patients studied [19].

Leukopenia was noted in 22 (44%) of our patients, whereas in the study by Banerjee M et al none of the 50 cases of DF manifested leucopenia [19]. In a study by Lin SF et al the incidence of leucopenia was 76% in patients with dengue fever [21].

Thrombocytopenia was observed in 48 (96%) of the patients in our study. Saquib MA et al in their study reported an incidence of 93% of thrombocytopenia in their study involving 556 seropositive patients during the 2011 dengue fever epidemic in Lahore, Pakistan [13]. Turbadkar D et.al in their study of 212 patients

reported an incidence of 76.74% of thrombocytopenia [16]. Kariyawasam S et al reported a 100% incidence of thrombocytopenia in their study involving 15 pregnant patients who were seropositive for DF[18].

Fatima S et al reported thrombocytopenia to the tune of 89% in their study involving a total of 131 seropositive patients [22]. Khan MU et al in their study quoted a 67.2% thrombocytopenia among 210 seropositive dengue positive patients[23]. Khan M et al reported an incidence of 71% thrombocytopenia[24].

## Conclusion

Dengue has evolved into a truly global arboviral illness with ever increasing multiple epidemics and a rising incidence of severity in the form of Dengue Haemorrhagic Fever throughout the tropics and subtropics with an impending risk of invading the temperate regions in this era of climate change and global warming.

Our study focused on the haematological changes in dengue fever in correlation with the clinical course.

It was concluded in this study that fever with headache in the presence of thrombocytopenia, leukopenia and reversal of neutrophil lymphocyte ratio should raise a strong suspicion of Dengue fever.

Thrombocytopenia and a rising haematocrit (PCV) by 20% from baseline were found to be important prognostic indicators during hospital stay and followup.

All patients with abnormalities in the clinical and haematological parameters in our study group made a complete recovery either during the hospital stay or within the follow up period.

Early suspicion, diagnosis and prompt management of Dengue fever will effectively lower any morbidity or mortality related to this dreaded illness.

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