

# An institution-based study on Hematological profile of Dengue patients at a tertiary care hospital in Konkan region of Maharashtra

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## Abstract

**Background:** Dengue is the most rapidly spreading mosquito-borne viral fever especially in coastal regions due to heavy rainfalls. It is important to understand the hemato-pathological changes associated with dengue infections to avoid dreaded hematological complications. These hematological changes can be used as diagnostic aid in remote rural set-ups wherein rapid dengue diagnostic kits are not available.

**Objective:** This retrospective study was carried out from 1<sup>st</sup> January 2018 to 31<sup>st</sup> August 2021 with an objective to analyze the hematological profile of serologically diagnosed dengue patients.

**Materials and Methods:** A cross sectional, observational, retrospective study was carried out at a tertiary care center at Dervan, Konkan region of Maharashtra over a period of three years and eight months. Commercially available 'Dengue Day 1 test kit' was used to detect NS1 antigen and IgM and IgG antibodies. Patients with positive NS1 antigen and/or IgM or IgG antibody were included while patients with other febrile illnesses like typhoid, malaria were excluded from this study. Patient's venous blood was collected in plain bulb for serology and in EDTA bulb for hematological profile (CBC/blood smear). This profile included hemoglobin, hematocrit (HCT), RBC indices like MCV, MCH And MCHC, total leucocyte count (TLC), Differential leucocyte count (DLC) and platelet count (PC).

**Results:** A total of 330 patients were diagnosed as dengue cases based on rapid card test. Majority of the patients were positive for NS1 antigen (60%) followed by IgM antibody (27.87%). Male: female ratio was 1.8:1. Age of the patients were in the range of 10-65 years whereas majority of NS1 positivity was seen in the age group of 21-30 years. Hemoglobin levels among these patients ranged from 3.1-19.9 g/dl. 27.47% cases had hemoglobin level of more than 15 g/dl and 16.96% patients had hemoglobin level <10 g/dl. 225 out of 330 patients showed hematocrit (HCT) >35% above the average reference value. HCT ranging from 20-35% was seen in 72/330 (21.82%) patients. 143/330 (43.34%) cases showed TLC <4000/cumm (leukopenia). 51.07% patients showed relative lymphocytosis with 15.15% of these cases showing reactive lymphocytosis. Maximum cases showed thrombocytopenia (69.32%). 31.21% showed grade 1 thrombocytopenia that is, platelets between 75000-150000/cumm. This grade was followed sequentially by Grade III, II and IV thrombocytopenia cases.

**Conclusion:** This study highlights important hematological parameters on different serological dengue diagnosis made on rapid card test. This study will help diagnose dengue disease in remote, rural set-ups wherein rapid diagnostic kits are not available.

**Key Words:** Dengue, hematological profile, serology, kit

## Introduction

In the extensive list of tropical diseases, dengue is one of the most common disease among them. India has reported many outbreaks of dengue infection with the

advent of the monsoon period. Cyclical trend is seen with a peak in September to October of every year<sup>[1]</sup>.

Dengue is a rapidly spreading, acute, self-limited disease<sup>[2]</sup>. Dengue is an arbovirus belonging to

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flavivirus genus of Flaviviridae family. DEN-1, DEN-2, DEN-3 and DEN-4 are the four serotypes of dengue virus. This virus is an encapsulated RNA virus transmitted by bite of infected female *Aedes Aegypti* mosquito<sup>[3,4]</sup>.

Epidemics of febrile illnesses include typhoid, measles, leptospirosis, malaria and severe acute respiratory distress syndrome which can be confused with dengue due to similar clinical features.<sup>[5]</sup>

Dengue fever is an acute febrile illness with rapid high-grade fever, headache, peri-orbital, muscle and joint pain and maculo-papular rash followed by severe complications like lymphadenopathy, hepatomegaly and hemorrhage<sup>[3-5]</sup>.

Dengue is also described as 'break-bone fever' as it results in severe bone pain. This infection may be subclinical or symptomatic. Symptomatic infection is grouped into (1) Dengue fever (DF), (2) Dengue hemorrhagic fever (DHF) and (3) Dengue shock syndrome (DSS)<sup>[6]</sup>.

Clinical course of DHF consists of three stages<sup>[7-9]</sup>. (1) Febrile phase (lasting 2-7 days), (2) Critical phase (leaking phase) (24-48 hours), (3) Convalescent phase (2-4 days).

Clinical diagnostic criteria of DHF by WHO is based upon: Sustained high grade fever lasting 2-7 days, Petechia or epistaxis with a positive tourniquet test, Thrombocytopenia (platelet count  $\leq 100 \times 10^9/L$ ) and Evidence of plasma leakage-hemoconcentration (an increase in hematocrit  $\geq 20\%$  above average for age, sex and population), pleural effusion and ascites<sup>[10]</sup>.

Early recognition and prompt management is required to decrease the morbidity and mortality of illness in Dengue cases. This pioneer study in a tertiary care hospital in Konkan region of Maharashtra aims to study the hematological profile of serologically diagnosed dengue patients and to know the rapid card test results.

**Materials and Methods**

A cross sectional, observational, retrospective study was carried out at our hematology section at a tertiary care hospital in Dervan, Konkan region of coastal Maharashtra over a period of three years and eight months (1<sup>st</sup> January 2018 to 31<sup>st</sup> August 2021).

Inclusion and Exclusion criteria:

Inclusion criteria: Patients with positive NS1 antigen and/or IgM or IgG antibody.

Exclusion criteria: Patients with other febrile illnesses like typhoid, malaria which coexisted with dengue positive serology were excluded from the study.

Commercially available 'Dengue Day 1 test kit' was

used to detect NS1 antigen and IgM and IgG antibody [Refer Figure 1].



**Figure 1:** Dengue day 1 kit test result showing NS1 antigen and IgM Ab positive. Control strand is also positive in each of the two kits. One kit is positive for NS1 antigen and other kit is positive for IgM and IgG Abs.

Our kit is produced by J. Mitra & Co. Pvt. Ltd. (New Delhi). Patients with positive NS1 antigen and/or IgM or IgG antibody were included in study while patients with other febrile illnesses like typhoid, malaria were excluded from this study. The clinical signs/symptoms were not taken into consideration in our cases.

Patients venous blood sample was collected in plain bulb for serology and in EDTA bulb for hematological profile. Hematological profile included hemoglobin, hematocrit (HCT), total leucocyte count (TLC), RBC indices, Differential leucocyte count (DLC) and platelet count (PC) of total 330 dengue positive patients.

**Results**

A total of 330 patients were diagnosed as dengue cases based on rapid card test.

**Table 1:** Distribution of patients based upon results of rapid Dengue kit test

Dengue test positive	No of cases	Percentage (%)
NS1	198	60
IgM	92	27.87
IgG	3	0.9
IgM & NS1	25	7.5
IgM & IgG	10	3
NS1 & IgG	1	0.3
NS1, IgM, IgG	1	0.3
Total	330	100

Based on rapid card test, the majority of the patients were positive for NS1 antigen (60%), IgM antibody (27.87%) and a combined positivity of IgM & NS1 (7.5%) (Table 1).

**Table 2:** Distribution of patients according to Gender and Dengue positive cases

Gender	Percentage (%)	NS1	IgM	IgG	IgM & NS1	IgG & IgM	NS1 & IgG	NS1, IgG, IgM	No. of cases
Males	64.24	135	51	1	18	6	0	1	212
Females	35.75	63	41	2	7	4	1	0	118
Total	100	198	92	3	25	10	1	1	330

Majority of the patients were males compared to females.

Out of 330 total patients, 212 were males and 118 were females. Both showed predominantly NS1 positivity and IgM positivity respectively. Male: female ratio is 1.8:1. (Table 2).

**Table 3:** Distribution of patients according to Age range and Dengue Kit results

Age (yrs)	Percentage (%)	NS1	IgG	IgM	IgM & NS1	IgG & IgM	NS1 & IgG	NS1,IgM, IgG	No. of cases
0-10	2.42	4	0	2	2	0	0	0	8
11-20	17.27	31	0	19	5	1	1	0	57
21-30	26.36	61	1	19	5	1	0	0	87
31-40	20.9	44	1	16	6	2	0	0	69
41-50	10.6	22	1	7	4	1	0	0	35
51-60	12.12	20	0	18	2	0	0	0	40
>60	10.3	16	0	11	1	5	0	1	34
Total	100	198	3	92	25	10	1	1	330

The majority of cases were in age group, that is, 21-30 years (26.36%) and were predominantly NS1 positive followed by IgM positive. 31-40 years of age group showed 69 cases with 20.9% positivity. Least number of cases (2.42%) were found in pediatric age group (0-10 years) (Refer Table 3).

**Table 4:** Distribution of patients according to hemoglobin concentration in Dengue positive results

Hb (gm/dl)	Percent (%)	NS1	IgG	IgM	IgM & NS1	IgG & IgM	NS1 & IgG	NS1,IgM, IgG	No. of cases
<10	7.87	3	0	19	1	3	0	0	26
10-12	16.96	22	2	26	3	3	0	0	56
12-15	47.87	104	1	38	10	4	0	1	158
>15	27.47	69	0	9	11	0	1	0	90
Total	100	198	3	92	25	10	1	1	330

Range of haemoglobin percentage was from <10 gm/dl to highest >15gm/dl. Haemoglobin range 12-15gm/dl showed maximum no. of cases, i.e. 158 out of 330 (47.87%) which showed predominantly NS1 positive followed by IgM positive. Least number of cases were found within haemoglobin range of <10gm/dl, i.e. 26 cases only out of 330 (7.87%) (Table 4).

**Table 5:** Distribution of patients according to hematocrit (%)

HCT (%)	Percent (%)	NS1	IgG	IgM	IgM&NS1	IgG& IgM	NS1&IgG	NS1,IgG,IgM	No. of cases
<20	10	6	0	22	1	4	0	0	33
20-35	21.82	20	2	41	5	4	0	0	72
>35	68.18	172	1	29	19	2	1	1	225
Total	100	198	3	92	25	10	1	1	330

In 225 out of 330 dengue patients (68.18%) showed hematocrit (HCT) >35% above the average reference value, which were NS1 positive predominantly followed by IgM. HCT ranging from 20-Around 35% was seen in 72/330 (21.82%) patients which showed IgM positive predominantly followed by NS1. While 33/330 (10%) dengue patients showed <20% HCT which also showed IgM positive predominantly followed by NS1 (Table 5).

**Table 6:** Distribution of patients according to total leucocyte count (TLC) (cells/cumm)

WBC Count (/cumm)	Percent (%)	NS1	IgM	IgG	IgM & NS1	IgM & IgG	NS1&IgG	NS1,IgM, IgG	No. of cases
<4000	43.34	109	15	0	15	4	0	0	143
4000-11,000	48.18	83	56	3	10	5	1	1	159
>11,000	8.48	6	21	0	0	1	0	0	28
Total	100.00	198	92	3	25	10	1	1	330

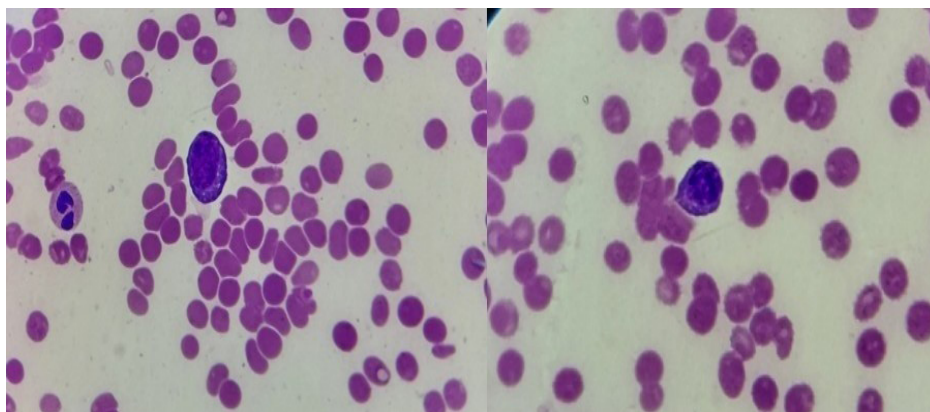
RBC count <3 millions/cumm was observed in 4.54% dengue cases. RBC count between 3-4 millions/cumm was seen in 16.36% cases. 4-5 millions/cumm RBC count was observed in 48.18% cases. 30.9% dengue cases had RBC count of >5 millions/cumm.

MCV <80 fl was seen in 20% of dengue cases. 76.96% of patients showed MCV between 80-100 fl and >100 fl MCV was observed in 3.3% of cases

About 17.57% of cases showed MCH <27 picogram (pg). Maximum dengue patients (70.9%) had MCH between 27-32 pg. >32 pg MCH was seen in 11.51% of patients.

MCHC >35g/dl was seen in 28.78% cases. 69.69% cases had MCHC between 31-35g/dl and 1.50% cases showed <31g/dl.

TLC ranging from 4000-11000/cumm showed maximum cases (48.18%) with 159 out of 330 showing NS1 positivity followed by IgM. 143 cases showed TLC <4000/cumm showing NS1 positivity followed by IgM positivity with 43.33% of total cases. Least no. of cases (8.48%) showed TLC >11000/cumm which also showed predominantly IgM positivity (Table 6).



**Figure 2:** Microphotograph split image showing reactive lymphocytes on peripheral blood smear (field stain, 400x)

About 51.07% patients showed relative lymphocytosis with 15.15% of these cases showing reactive lymphocytosis (Figure 2).

**Table 7:** Distribution of patients according to platelet count

Platelet count	NS1	IgG	IgM	IgM & NS1	IgG & IgM	NS1 & IgG	NS1, IgM, IgG	Percent (%)	No. of cases
Thrombocytopenia (<1.5 lakhs/cumm)	150	2	45	22	8	1	1	69.32	229
Within normal limit (1.5-4.5 lakhs/cumm)	47	1	42	3	1	0	0	28.48	94
Thrombocytosis (>4.5 lakhs/cumm)	1	0	5	0	1	0	0	2.20	7
Total	198	3	92	25	10	1	1	100	330

In 33.93% of patients showed differential leucocyte count within normal limits while neutrophilia was seen in 12.3% of cases, 1.8% showed eosinophilia, while 0.9% showed monocytosis.

Thrombocytopenia was seen in 69.32% of cases which were NS1 positive while only 2.2% of cases showed thrombocytosis while rest of the cases were within normal limit (28.48%) (Table 7).

**Table no 8:** Distribution of 229 cases of Dengue with thrombocytopenia : based upon thrombocytopenia grades (Gr)

Platelet count	Percent (%)	NS1	IgG	IgM	IgM & NS1	IgG & IgM	NS1 & IgG	NS1, IgG, IgM	Total
75,000-1,50,000 (Gr I)	31.21	66	1	20	10	5	1	0	
50,000-75,000 (Gr II)	12.12	27	0	8	4	1	0	0	
25,000-50,000 (Gr III)	17.81	44	1	9	4	1	0	0	
<25,000 (Gr IV)	8.18	13	0	8	4	1	0	1	
Total	69.32	150	2	45	22	8	1	1	229

Around 31.21% of dengue cases showed Grade I thrombocytopenia followed sequentially by Grade III, II and IV thrombocytopenia (Table 8).

**Discussion**

The word ‘dengue’ is presumed to have originated from Swahili language “ki denga pepo”, meaning ‘sudden cramp-like seizure’. According to the WHO, almost 50 million people get dengue infection annually. WHO estimates almost half of the world’s population lives in countries having endemicity for dengue infection<sup>[11]</sup>. So we conducted this study at our set-up.

Our study showed that maximum 198/330 (60%) dengue positive cases were NS1 positive followed by 92/330 cases (27.87%) IgM positive cases. This finding was in accordance with study done by Dongre T, et.al. (2015)<sup>[12]</sup> which showed 59.80% NS1 positive cases followed by IgM positivity in 16.26% cases.

Out of 330 cases 212 (64.24%) were males and 118 (35.75%) were females with male to female ratio of 1.7:1. Most of these patients were in adult age group. In a study done by Babuji A, et.al. (2020)<sup>[11]</sup>, the male: female ratio was found to be 1.7: 1 which was close to our study (1.8:1).

Most affected age group in our study was 21-30 years with 26.36% dengue positive cases. Study of Babuji A, et.al. (2020)<sup>[11]</sup> showed similar age group affected with 31.4% dengue positive cases.

Leucopenia is the most prominent hematological change in dengue cases. In our study, leucopenia was seen in 43.34% while leukocytosis was seen in 8.48% dengue cases. In the study conducted by Kate MS, et.al, (2017)<sup>[13]</sup>, leucopenia was seen in 35.08% dengue cases and leukocytosis in 12.28% cases.

Anemia is seen in dengue fever due to ongoing hemolysis in peripheral blood. Hemoglobin (gm/dl) concentration was decreased (<12g/dl) in 24.83% of our dengue positive cases. Increased Hb (>15g/dl) was seen in 27.27% cases. Babuji A, et.al, (2020)<sup>[11]</sup> showed decrease in hemoglobin (gm/dl) concentration in 35.85% of their dengue positive cases and increase in hemoglobin (gm/dl) concentration in 21.14% of their cases.

Low platelet count is seen in dengue cases. Our study showed thrombocytopenia in 69.32% of dengue positive cases while Dongre T, et.al, (2015)<sup>[12]</sup> showed thrombocytopenia in 53.88% of their cases. Study by Mohan K, et.al, (2021)<sup>[14]</sup> showed thrombocytopenia in 24% of their dengue positive cases. 31.21% of our dengue cases showed Grade I thrombocytopenia followed sequentially by Grade III, II and IV thrombocytopenia. This grading was not done by other studies. Most studies recorded thrombocytopenia as mild/moderate/severe.

Rising value of hematocrit is marker of the critical phase of dengue infection. Raised hematocrit was seen in 60% of our dengue cases. Mohan K, et al. (2021)<sup>[14]</sup> recorded hematocrit (>35%) as 7.6% in their dengue cases. Khatroth S, et al. (2017)<sup>[15]</sup> recorded the same in 30 out of their 60 cases (50% of their dengue cases)

**Conclusion**

Dengue cases are more prevalent in Konkan region due to heavy rainfalls in coastal Maharashtra and stagnant waters, needing epidemiological studies for the same. Clinical correlation to laboratory findings is a must for appropriate treatment. Maximum NS1 antigen positivity in most of our cases denote patients presented early at our set-up for management. NS1 positive cases, increased hematocrit, low Hb, Leucopenia with reactive lymphocytosis and thrombocytopenia were the prominent findings in our study. The blood picture can be a clue to the severity/diagnosis of dengue fever. Early diagnosis leads to prompt treatment and prevents dreadful complications like Dengue hemorrhagic fever and Dengue shock syndrome.

**Limitation:** This is purely a hemato-pathological study done on dengue cases. Clinical details were not recorded at the time of presentation of our dengue patients in our lab.

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