

**Original article:**

## **An Analysis of Hematological Parameters as a Diagnostic test for Dengue in Patients with Acute Febrile Illness**

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### **ABSTRACT**

**INTRODUCTION:** Haematological changes are among the most common complications encountered in dengue. This study analyzes and statistically evaluates the haematological changes as a diagnostic test for dengue in patients with acute febrile illness and whether these could guide the clinician for further management.

**MATERIAL AND METHODS:** This is a prospective study carried out on 200 cases of dengue fever from January 2014 to November 2015. A complete blood count and serology for dengue were performed. Exclusion: malaria, enteric fever, chikungunya, respiratory infections.

**RESULTS:** Out of 200 patients, 132 males and 68 females with M:F=1.94:1. The mean age of these patients was 28.3 years and the highest proportion was seen in the age group of 20-29 years (53%). Most common abnormal laboratory finding is thrombocytopenia present in 158 patients out of total 200 patients followed by atypical lymphocytosis in 140 patients, leucopenia in 112 patients, HCT ( $\geq 45\%$ ) in 28 patients, S. creatinine ( $>1.2\text{mg\%}$ ) in 16 patients, Hb ( $\leq 10\text{gm\%}$ ) in 14 patients, 08 patients had PT ( $>14\text{sec}$ ), 08 had aPTT ( $>40\text{sec}$ ) & 08 had INR ( $>1.2$ ).

**CONCLUSION:** This study revealed that routinely used laboratory findings such as haemoglobin, leukocytes, platelet counts and even atypical lymphocytosis can provide a diagnostic clue in a patient with acute febrile illness in endemic areas, thus increasing the probability of dengue and enhancing prompt initiation of treatment.

**KEYWORDS:** Dengue, Haematological parameters, Atypical lymphocytosis

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### **INTRODUCTION:**

Dengue continues to be a major health problem in some of the most populated areas of the world. It is one of the important causes of febrile illnesses in our part of the world. Dengue is the most rapidly spreading mosquito-borne viral disease of mankind, with a 30-fold increase in global incidence over the last five decades. Almost half the world's population lives in countries where dengue is endemic. According to WHO, about 50-100 million new dengue infections are estimated to occur annually in more than 100 endemic countries, with a steady

increase in number of countries reporting the disease.<sup>1</sup>

### **GLOBAL SCENARIO**

➤ Dengue has been identified as one of the 17 neglected tropical diseases by WHO as mentioned in their first report on neglected tropical diseases (2010).<sup>2</sup>

➤ Although the full global burden of the disease is still uncertain, the patterns are alarming for both human health and the economy. Every year, hundreds of thousands of severe cases arise, of which 20000 lead to death. The loss to the economy is 264

disability-adjusted life years (DALYs) per million population per year.<sup>3,4</sup>

➤ Approximately 1.8 billion (more than 70%) of the population at risk for dengue worldwide live in Member States of the WHO South-East Asia Region (SEAR) and Western Pacific Region, which bear nearly 75% of the current global disease burden due to dengue.<sup>5</sup>

➤ Of the 11 countries of SEAR, 10 countries including India are endemic for Dengue. The only exception is the Democratic People's Republic of Korea. In 2012, SEAR countries reported approximately 0.29 million cases, of which Thailand contributed almost 30%, Indonesia 29%, India 20%. Similarly, Western Pacific countries have reported 0.33 million cases, of which Philippines contributed almost 52%, Vietnam 24% and Cambodia 14% (source WHO).<sup>5</sup>

➤ The true numbers are probably far more, since severe underreporting and misclassification of dengue cases have been documented by the countries.<sup>3</sup>

#### **NATIONAL SCENARIO**

➤ Dengue virus was isolated in India for the first time in 1945. The first evidence of occurrence of dengue fever in the country was reported in 1956 from Vellore district in Tamilnadu. The first dengue hemorrhagic fever (DHF) outbreak occurred in Calcutta (West Bengal) in 1963.<sup>6,7</sup>

➤ Of the 36 states/UTs, 35 (all except Lakshadweep) have reported dengue cases during the last two decades. Recurring outbreaks of dengue fever (DF)/DHF have been reported from various states/UTs-Andhrapradesh, Chandigarh, Delhi, Goa, Haryana, Gujarat, Karnataka, Kerala, Maharashtra, Rajasthan, Uttarpradesh, Puducherry, Punjab, Tamilnadu, and West Bengal. During 1996, one

of the most severe outbreaks of DF/DHF occurred in Delhi, with 10252 cases and 423 deaths being reported (country total being 16517 and 545 deaths). In 2006, the country witnessed an outbreak of DF/DHF with 12317 cases and 184 deaths. The incidence of dengue is increasing in the last few years. During 2010, a total of 28292 cases were reported, which increased to 50222 in 2012 and 75808 in 2013-the highest since 1991. The case fatality ratio (CFR-deaths per 100 cases) has declined from 3.3% in 1996 to 0.4% in 2010 after the national guidelines on clinical management of DF/DHF/dengue shock syndrome (DSS) were developed and circulated in 2007. This further declined to 0.3% in 2013.<sup>7,8</sup>

➤ Every year, during the period July-November, an upsurge in the cases of dengue/DHF has been observed. The disease has a seasonal pattern; the cases peak after the monsoons and are not uniformly distributed throughout the year. However, the states in the southern and western parts of the country report perennial transmission.

#### **VECTOR**

➤ Dengue viruses are transmitted from an infected person to others by the bite of the female Aedes (Ae.) mosquito. In India, Ae. Aegypti is main vector in most urban areas; however, Ae. Albopictus is also incriminated in many states. Other species like Ae. Polynesiensis and Ae. Niveus have also been incriminated as secondary vectors in some countries.

➤ The female Aedes mosquito deposits eggs singly on damp surfaces just above the waterline. Under optimal conditions, the adult emerges in seven days (after the aquatic stages in the life cycle of Ae.

Aegypti). At low temperatures, it may take several weeks to emerge. The eggs can withstand desiccation (can remain in a viable dry condition) for more than a year and emerge within 24 hours once it comes in contact with water. This is also a major hurdle in prevention and control of dengue.

- Climatic conditions, particularly temperature and rain fall, have a major impact on the life cycle, breeding and longevity of vectors and thus transmission of the disease. The average survival of *Ae. Aegypti* is 30 days and *Ae. Albopictus* is about eight weeks. During the rainy season, when survival is longer, the risk of virus transmission is greater. *Aedes* is a daytime feeder and can fly up to a limited distance of 400 metres. In the absence of any vaccine or specific drug for dengue, vector control is very significant in preventing disease transmission.
  - *Ae. aegypti* breeds almost entirely in domestic man-made water receptacles found in and around households, water storage containers, water reservoirs, overhead tanks, desert coolers, unused tyres, coconut shells, disposable cups, unused grinding stones, industrial and domestic junk, construction sites, etc.
  - *Ae. Albopictus* prefers natural larval habitats which include tree holes, latex cups in rubber plantations, leaf axils, bamboo stumps, coconut shells, etc. However, *Ae. Albopictus* breeding has been reported recently in domestic habitats as well.
- The clinical diagnosis of Dengue is challenging because of the non-specific nature of the signs and symptoms, which

overlap considerably with other febrile illnesses common in tropical regions and availability & durability of dengue virus specific test is also an issue in tropical regions. As virus induces haematological alterations; prediction of the haematological changes enables the clinicians to establish an effective and early therapeutic intervention in order to prevent the occurrence of major complications.

Haematological abnormalities that have been reported with Dengue include anaemia, leucopenia, thrombocytopenia, atypical lymphocytosis and disseminated intravascular coagulation.

#### **MATERIAL AND METHODS:**

This is a prospective study carried out on 200 cases of dengue fever admitted in tertiary care hospital from January 2014 to November 2015. The case definition is based on compatible clinical history and examination based on WHO criteria, confirmed by positive serology to dengue fever.

Patients those who are more or equal 12 years of age and those admitted with fever, headache, myalgia are evaluated with other clinical features (warning signs of dengue fever, signs of haemorrhage, signs of plasma leakage and signs of shock). Laboratory investigations such as Hb, total count, differential count, platelet count, packed cell volume, peripheral smear for malarial parasite, and liver function test (including S.protein) and renal function test are carried out. Blood coagulation profile such as Bleeding Time, Clotting Time, Prothrombin Time and aPTT are carried out.

Other causes of fever like malaria, enteric fever, chikungunya and respiratory infections are excluded by appropriate tests.

## RESULTS:

A total of 200 cases of dengue have been included in this study as confirmed by the serology for dengue (NS1, Ig M, Ig G). It was revealed that out of 200 cases, 172 cases had NS1 positivity, 12 cases had Ig M positivity, 04 cases had Ig G positivity and 12 cases had mixed (NS1±Ig M±Ig G) positivity.

The positive dengue group was composed of 132 males and 68 females with male to female ratio of 1.94:1. The mean age of these patients was 28.3 years and the highest proportion was seen in the age group of 20-29 years (53%).

## ABNORMAL LABORATORY FINDINGS IN DENGUE PATIENTS:

As shown in table – 1 we observed that most common abnormal laboratory finding is thrombocytopenia present in 158 patients out of total 200 patients followed by atypical lymphocytosis in 140 patients, leucopenia in 112 patients, HCT ( $\geq 45\%$ ) in 28 patients, S. creatinine ( $>1.2\text{mg}\%$ ) in 16 patients, Hb ( $\leq 10\text{gm}\%$ ) in 14 patients, 08 patients had PT ( $>14\text{sec}$ ), 08 had aPTT ( $>40\text{sec}$ ) & 08 had INR ( $>1.2$ ).

**THROMBOCYTOPENIA:** As shown in table – 2 we observed that in our study thrombocytopenia is common in dengue patients. At the time of initial presentation 20% patients had platelet count more than  $1,00,000/\mu\text{l}$ , 38% of patients had a platelet count was between  $50,000-1,00,000/\mu\text{l}$ , 34% patients had platelet count between  $20,000-49,999/\mu\text{l}$ , severe thrombocytopenia (platelet count between  $10,000-19,999/\mu\text{l}$ ) seen in 6% patients and only 2% patients had very low platelet count ( $<10,000/\mu\text{l}$ ).

**DISCUSSION:** Dengue is a major health problem in the tropic regions of world which poses a significant burden on health expenditure. In India, it is not just confined to the rural areas but is also rampant in the

urban locales. Prompt and accurate diagnosis is critical towards the effective management of dengue.

The current study of 200 patients shows that the mean age of these patients was 28.3 years and the highest proportion was seen in the age group of 20-29 years (53%). Findings were in accordance with other studies like Chakravarti and Kumaria<sup>10</sup>; Gupta et al.<sup>11</sup>; Kolkata study<sup>12</sup> other than Kerala study. Age difference in present study and Kerala study is due to outbreak of dengue in Kerala at that time (Table-3). Male to female ratio was 1.94:1 with male predominance in other studies like Kerala study<sup>9</sup>, Chakravarti and Kumaria<sup>10</sup>, Gupta et al.<sup>11</sup>, Kolkata study<sup>12</sup> also observed male predominance.

## ABNORMAL LABORATORY FINDINGS IN DENGUE PATIENTS:

In present study most common abnormal laboratory finding was **Thrombocytopenia** ( $<11\text{lac}/\mu\text{l}$ ) present in 158 patients (79%) out of total 200 patients followed by atypical lymphocytosis leucopenia, HCV ( $\geq 45\%$ ), S. creatinine ( $>1.2\text{mg}\%$ ), Hb ( $\leq 10\text{gm}\%$ ) and PT ( $>14\text{sec}$ ), aPTT ( $>40\text{sec}$ ), INR ( $>1.2$ ). Other studies like Ageep AK et al<sup>13</sup> (88%); Mittal H et al<sup>14</sup> (92.6%) & Seema A et al<sup>15</sup> (84%) also shows similar results.

**Leucopenia** present in 56% cases in our study (table VI, figure 12). In study of Itoda et al, in Japan (2006)<sup>16</sup> leucopenia was detected in 71% cases.

**Increased HCT** present in 14% cases in our study (table VI, figure 12). In USG based study in Thail and, by Kalayanarooj S et al (1997)<sup>17</sup> increased HCT were present in 18% cases and in Bangladesh based study by Mia MW et al (2010)<sup>18</sup> increased HCT were present in 27% cases.

Findings were in accordance with other studies.

**CONCLUSION:** Overall, the haematological aspects of dengue constitute a very interesting area. We concluded that routinely used laboratory findings

such as anaemia, thrombocytopenia, leucopenia in association with atypical lymphocytosis can provide a diagnostic clue in a patient with acute febrile illness in endemic areas. Because of limitation of resources and trained health personnel in much of the dengue infested areas, presumptive clinical diagnosis seems a relevant option.

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**TABLE – 1: ABNORMAL LABORATORY FINDINGS IN DENGUE PATIENTS (n=200)**

Laboratory findings	No. of patients	Percentage (%)
Hb ( $\leq 10$ gm%)	14	7
Leucopenia ( $< 4000/\mu\text{l}$ )	112	56
Thrombocytopenia ( $< 1.0$ lac/ $\mu\text{l}$ )	158	79
HCT ( $\geq 45$ %)	28	14
Atypical Lymphocytosis	140	70
PT ( $> 14$ sec)	08	4
aPTT ( $> 40$ sec)	08	4
INR ( $> 1.2$ )	08	4
S.creatinine ( $> 1.2$ mg%)	16	8

**TABLE – 2: THROMBOCYTOPENIA**

Platelet count ( $\mu\text{l}$ )	No. of patients	Percentage (%)
$< 10,000$	04	2
10,000-19,999	12	6
20,000-49,999	68	34
50,000-1,00,000	76	38
$> 1,00,000$	40	20
Total	200	100

**TABLE – 3: COMPARISON STUDY OF AGE GROUPS**

Author	Year	Common age group
Kerala study <sup>9</sup>	2005	31-50
Chakravarti and Kumaria <sup>10</sup>	2005	21-30
Gupta et al. <sup>11</sup>	2006	21-30
Kolkata study <sup>12</sup>	2013	11-30
Present study	2015	20-29

**TABLE – 4: COMPARISON OF THROMBOCYTOPENIA**

Author	Year	Percentage (%)
Ageep AK et al <sup>13</sup>	2006	88
Mittal H et al <sup>14</sup>	2012	92.6
Seema A et al <sup>15</sup>	2012	84
Present study	2015	79

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