

Hematological Parameters in Dengue Fever: A Study in Tertiary Care Hospital

Rajiv Ranjan Singh¹, Renu Kumari², Ajit Kumar Chaudhary³

¹Tutor, Department of Pathology, Darbhanga Medical College and Hospital, Laheriasarai, Bihar

²Tutor, Department of Physiology, Darbhanga Medical College and Hospital, Laheriasarai, Bihar

³Professor and Head of Department, Department of Pathology, Darbhanga Medical College and Hospital, Laheriasarai, Bihar

Received: 25-06-2023 / Revised: 28-07-2023 / Accepted: 30-08-2023

Corresponding author: Dr. Renu Kumari

Conflict of interest: Nil

Abstract:

Background: Humans contract the dengue virus through the bite of an infected mosquito. The severity of this condition is predicted using a variety of clinical and laboratory criteria. The study aim was to ascertain the hematological parameters in dengue fever patients.

Methods: Serology was performed on 100 cases that had a confirmed diagnosis of dengue. Complete blood count, coagulation profile, and liver function tests were performed, along with a thorough history, physical exam, and investigation. They were observed during their hospital stay and afterward.

Results: The prevalence of dengue infection was higher in the adult age group, with a slight male predominance. With other constitutional symptoms, dengue fever was the most frequent presentation. The most frequent clinically evoked symptom was petechial ecchymosis. In the majority of patients, hematological abnormalities including elevated hemotocrit, platelet count, and unusual lymphocytes were observed. The mainstay of management was supportive therapy. 2% of the cases had overall mortality.

Conclusion: Early detection of Dengue infection will be aided by elevated hematocrit, thrombocytopenia, leucopenia, and atypical cells in the peripheral smear. For a good outcome of the condition, early detection and prevention of complications are more crucial than treatment.

Keyword: Dengue fever, Platelet count, Leucopenia, Dengue serology.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

The most prevalent flavivirus in tropical and subtropical areas is dengue. [1,2] In India, it is also a significant health issue. 33 million clinically detectable dengue cases, or one-third of all dengue cases worldwide, are reported each year in India, according to statistics from the Global Model. [3]

Female *Aedes aegypti* mosquitoes and, to a lesser extent, *Aedes albopictus* mosquitoes are the main carriers of the disease. Extracellular matrix (ECM), membrane, and nuclear capsid (DENV) proteins are all encoded by positive-strand RNA viruses.

Dengue virus has four different serotypes: DEN-1, DEN-2, DEN-3, and DEN-4. [4]. The mosquito vector has an 8–12 day extrinsic incubation period, a 3–14 day intrinsic incubation period, and an approximately 7 day infectivity period. [5]

Clinical symptoms of dengue include fever, headache, pain behind the eyes, overall weakness, and either nausea or vomiting. Dengue shock syndrome (DSS) and dengue haemorrhagic fever (DHF) are manifestations of leakage of arteries

lined with defective endothelial cells, which might worsen bone marrow suppression. These potentially fatal consequences are thought to be caused by the generation of inflammatory cytokines, including immune-mediated reactions. Clinical, epidemiological, and laboratory data are used to make the diagnosis. There are two types of laboratory tests: non-specific (blood tests) and specific (isolation and serological tests to find IgG, IgM, and NS1 antibodies and antigens).

DNA sequence-based amplification (NASBA), an RNA-specific isothermal amplification test that does not require thermal cycling, is the gold standard for DF detection. Particularly *Aedes albopictus* C6/36 or AP61 (*Aedes pseudoscutellaris*) virus cultures are employed. The NASBA method and virus culture, on the other hand, need a lot of time, money, and work. In order to save time and money, card tests are used to diagnose dengue. The new standard has been replaced by RT-PCR and ELISA because of their excellent specificity and sensitivity. [6]

Material and Methods

This prospective study was conducted at Department of Pathology, Darbhanga Medical College, Laheriasarai, Bihar from August 2019 to November 2019. The study included all patients of both sexes older than 15 years old who had been hospitalized to medicine wards and had a confirmed case of dengue fever using an IgM/IgG ELISA test. The study excluded all adult patients who tested negative for dengue IgM/IgG by ELISA.

On a predesigned and pretested proforma, demographic information including age, gender, address, and occupation were collected.

At the time of admission, all baseline tests, including the complete blood count, coagulation profile, liver function test, renal function test, X-ray chest, and abdominal ultrasound, were performed.

The baseline (normal) hematocrit of each patient was determined by the point at which their hemodynamic condition and hematocrit stabilized during their recovery. The following ratio was derived to assess the patients' level of hemoconcentration. [7]

$$\left[\frac{\text{Highest HCT} - \text{Recovery HCT}}{\text{Recovery HCT}} \right] \times 100$$

Hemoconcentration of at least 20% was regarded as being substantial. These estimations did not include patients whose bleeding was severe enough to

reduce their hematocrit. Centrifuging blood samples for serological testing allowed for the identification of IgM antibodies using MAC ELISA. Based on the WHO's technical recommendations, the severity of each case was rated using specific criteria. [8-10] Descriptives, Frequencies, Crosstabs, Chi-Square Test were used.

The Statistical software namely SPSS (version 16.0) and Minitab (version 11.0) were used for the analysis of the data and Microsoft word and Excel have been used to generate tables.

Results

The male to female ratio was 3:1, the majority (32%) of the patients were in the 15 to 25 year age range, and the fewest patients were beyond the age of 55. The most typical presenting symptom was a fever, which was followed by vomiting, back pain, and myalgia. Dengue fever was present in 54 percent of patients who had been exposed to the virus at the time of admission; 17 (17%) of these patients had DHF Grade I, 12 (12%) had DHF Grade II, and 17 (17%) had DSS, which is DHF Grade III + Grade IV.

The mean temperature among the dengue patients during the hospital stay had decreasing trend. Out of 100 patients, 15 (15%) had hematocrit levels > 20%, 57 (57%) had < 20% and 28 (28%) had normal hematocrit and the results were statistically significant. Thrombocytopenia in 97% of patients as seen in Table 1.

Table 1: Platelet count on admission day

Platelet count (/mm ³)	No. of cases	Percentage
<10,000	12	12.0%
10,000-20,000	29	29.0%
20,000-50,000	42	42.0%
50,000-1,00,000	14	14.0%
>1,00,000	3	3.0%
Total	100	100.0%

Leucocyte count was normal in majority of the cases as seen in Table 2.

Table 2: Leucocyte count on admission day

Leucocyte count (/mm ³)	No. of cases	Percentage
<4,000	22	22.0%
4,000-11,000	62	62.0%
>11,000	16	16.0%

Chi-square (X^2) = 37.520, DF=2, p=0.000. In 97% of the cases, peripheral smears revealed abnormal cells. Out of 100 individuals in the current study, 53 (or 53%) had normal liver function tests and 47 (or 47%) had abnormal liver functions. APTT was normal in 64 (64%) of the patients, increased in 36 (36%) of the patients, and the results were statistically significant ($P < 0.005$). As shown in Table 3, bleeding manifestations were frequently observed when the platelet count fell below 10,000/cu.mm³.

Table 3: Correlation between thrombocytopenia and bleeding

Platelet count	Bleeding manifestations		Without bleeding manifestation		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
<10,000	10	10.0%	2	2.0%	12	12.0%
10,000-20,000	11	11.0%	18	18.0%	29	29.0%
20,000-50,000	18	18.0%	24	24.0%	42	42.0%
50,000-1,00,000	5	5.0%	9	9.0%	14	14.0%
>1,00,000	2	2.0%	1	1.0%	3	3.0%
Total	46	46.0%	54	54.0%	100	100.0%

P-value=0.000. DHF 1, 2, 3, and 4 revealed positive IgG antibodies but classical dengue fever did not. During their hospital stays, dengue patients' mean platelet counts tended to rise (Table 4).

Table 4: Platelet trend during the hospital stay

Duration	Mean	SD
Day 1	36892.7835	28659.01272
Day 2	61333.3333	29993.87693
Day 3	89437.8947	38918.92604
Day 4	105242.4242	44510.34819
Day 5	120447.3684	54025.368.10
Day 6	127687.5000	56757.63532
Day 7	179666.6667	65178.72864

No deaths from dengue fever or dengue hemorrhagic fever of grades I, II, or III were reported in the current study. Two (2%) individuals with Grade IV dengue hemorrhagic fever passed away.

A platelet transfusion was given to the majority of patients (18%), followed by vitamin K administration (10%), fresh frozen plasma (5%) and steroid administration (3%) in that order.

Discussion

The gender ratio in the current study was similar to those in the investigations by Agarwal et al. [11] and Sharma et al. [12], with males being the most impacted. According to research by Sharma et al., [12] Rachel Daniel et al., [13] SK Agarwal et al., [14] and Eva Harris et al., [15] fever was the most typical manner of presentation. The most frequent presenting symptom in our study and those conducted by Sharma S et al [12] and Rachel Daniel et al [13] and Krishnamurthy K et al [16] was petechial/ecchymosis, although hepatomegaly was the most prevalent symptom in those studies. According to our study, Kalayanarooj S et al study, Eva Harris et al. study, and other studies, dengue virus infection manifests most frequently as dengue fever. [17] It is thought that hemoconcentration with a 20% or higher hematocrit rise is unmistakable proof of enhanced vascular permeability and plasma leakage. [18]

In the present study, Hct > 20% was present in 15 (15%) of cases and <20% in 57 (57%). A DHF epidemic in adults was documented in Delhi in 1996 by Sharma S et al [12], who found that Hct > 48% was observed in 6 (6.12%) individuals and Hct > 20% was reported in 14 (14.28%). In a study by Nazis et al. [19] and Joshi AA et al., the hematocrit was increased in more than half of the patients. 20 In one trial, only one patient (2.17%) had a higher hematocrit of more than 20%, while in another, DHF AND DSS experienced an increase in hematocrit levels of more than 45%. [22] In the present study a low Hct value is probably due to high prevalence of anemia in this region.

Thrombocytopenia (<1, 00,000/mm³) is one of the defining criteria for dengue haemorrhagic fever and

was seen in 97% of the cases in the present study, similar study done by Sharma S. et al, [12] Joshi AA et al, [20] Tahlan A et al [21] and Surendra Nath Singh Yadav. [23]

The overall leucocyte count was not significantly affected by dengue illness. According to the findings of the current investigation, the leucocyte count was normal in the majority of cases. Similar studies done by Krishnamurthy K. et al [16] and Joshi AA et al. [20] While the studies done by Nazish Butt et al, [19] Shamsunder Khatroth, [22] Surendra Nath Singh Yadav [23] and Meena KC et al [24] observed leucopenia in more than 50% of the cases. 94% of the cases showed leucopenia in a study done by Fu-Xi Qiu et al. [25] Peripheral smear showed atypical lymphocytes, few showing dark basophilic cytoplasm and large nucleus while few had plasmacytoid morphology. Similar observations were seen in studies done by Singh Yadav [23] and Choudhary et al. [26]

In 53% of cases, liver function tests were normal; in 47% of cases, they were abnormal. According to Sharma S. et al. [12], SGOT was elevated in 88.4% of cases, whereas SGPT was up in 76.7% of cases. Studies by Mohan et al., Deshwal et al., Kularatneet al., and Mandal et al. all reported increased liver transaminases of more than 80%. [27,28,29,30]

Out of 100 patients in our study, 64 (64%) had normal PT/APTTs and 36 (36%) had elevated PT/APTTs. In investigations conducted by Irfan Arshad, Choudhary et al., and Ayub et al. [26,31,32], respectively, prolonged APTT was observed in 26%, 20%, and 10% of cases. The majority of individuals whose platelet count fell below 20,000/mm³ displayed bleeding symptoms. But was further noted in patients whose platelet counts above 1 lakh/mm³. Therefore, the platelet count has no bearing on bleeding manifestation. An investigation done in Indonesia found similar results. [33] Six to seven days on average were needed for the platelet count to rise to levels that were close to normal. Out of 100 patients in the current study, 54 (54%) had just IgM positivity, of which 2 (2%) had dengue hemorrhagic fever. The remaining 44 (44%) patients all had dengue

hemorrhagic fever and had both IgM and IgG positive dengue serology. [32] IgM positive cases, 23 of whom had dengue hemorrhagic fever, were identified in a research conducted in Thailand [34] in 2000, as were 133 patients who tested positive for both IgM and IgG, of whom 53 had dengue hemorrhagic fever. Dengue fever is not known to have a specific therapy. Only 18 patients had platelet transfusions along with Vitamin K, fresh frozen plasma, and hydration therapy, despite the fact that 41% of the patients had platelet counts less than 20,000/mm³, on average. Even though steroids are not recommended for dengue fever, a small percentage of patients (3%), who received steroid therapy, showed signs of quick recovery and blood pressure stabilization.

In the current study, 2 (2%) out of 100 DF, DHF/DSS patients overall died. In grades I and II of DF and DHF, there was no mortality. Due to hypovolemic shock and respiratory failure, one patient in DSS passed away. Either as a result of DIC (disseminated intravascular coagulation) and acute renal damage. Therefore, early disease detection and prevention rather than therapy of consequences are crucial for the disease's successful course of treatment.

Conclusion

Hematological indicators, such as a decreased platelet count, an increased hemotocrit, a coagulation profile, and abnormal cells in peripheral smears, in conjunction with liver function tests and serology, aid in the early detection of dengue infection, thereby lowering the risk of complications and mortality.

References

- Halstead SB. The XXth century dengue pandemic: need for surveillance and research. *World Health Stat Q.* 1992; 45(2-3):292-8.
- Xu G, Dong H, Shi N, Liu S, Zhou A, Cheng Z. An outbreak of dengue virus serotype 1 infection in Cixi, Ningbo, People's Republic of China, 2004, associated with a traveller from Thailand and high density of *Aedes albopictus*. *Am J Trop Med Hyg.* 2007; 76:1182-88.
- Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. *Nature* 2013; 496(7446):504-7.
- Gubler DJ. Dengue and dengue hemorrhagic fever: its history and resurgence as a global public health problem. In: Gubler DJ, Kuno G, editors. *Dengue and dengue hemorrhagic fever*. London: CAB International. 1997:1-22.
- Tomashek KM, Margolis HS. Dengue: a potential transfusion-transmitted disease. *Transfusion.* 2011; 51(8):1654-1660.
- Shu PY, Huang JH. Current advances in dengue diagnosis. *Clinical and Diagnostic Laboratory Immunology.* 2004; 11(4):642-650.
- Cohen SN, Halstead SB. Shock associated with dengue infection. *J Pediatr.* 1966; 68(3):448-56.
- Nimmannitya S. Clinical manifestations of dengue/yellow haemorrhagic fever. In: WHO Regional Office for South-East Asia. *Monograph on dengue/dengue haemorrhagic fever*. New Delhi; 1993.
- Nimmannitya S, Halstead SB, Gohen SN, Margotta MR. Dengue and chikungunya virus infection in Thailand 1962-64: Observations on hospitalized patients with haemorrhagic fever. *Am J Trop Med Hyg.* 1969; 18:954-71.
- Kalayanarooj S, Vaughn DW, Nimmannitya S, Green S, Suntayakorn S, Kunentrasai N, et al. Early Clinical and Laboratory Indicators of Acute Dengue Illness. *J Infect Dis.* 1997; 176(2):313-21.
- Agarwal R, Kapoor S, Nagar R, Misra A, Tandon R, Mathur A, et al. A clinical study of the patients with dengue hemorrhagic fever during the epidemic of 1996 at Lucknow, India. *Southeast Asian J Trop Med Public Health.* 1999; 30(4):735-40.
- Sharma S, Sharma SK, Mohan A, Wadha J, Dar L, Thulkars. Clinical Profile of Dengue Hemorrhagic Fever in Adults during 1996-Outbreak in Delhi, India. *Dengue Bull.* 1998; 22:20-30.
- Daniel R, Rajamohanan, Philip AZ. A Study of Clinical Profile of Dengue Fever in Kollam. *Dengue Bull.* 2005; 29:197-202.
- Singh NP, Jhamb R, Agarwal SK. Outbreak of dengue fever in Delhi, India. *Southeast Asian J Trop Med Public Health.* 2003; 36(5):1174-8.
- Harris E, Videz E, Perez L, Sandoval E, Tellez Y, Perez ML, et al. Epidemiological and Virologic Features of Dengue in the 1998 Epidemic in Nicaragua. *Am J Trop Med Hyg.* 2000; 63:5-11.
- Krishnamurthy K, Kasturi TE, Chittipantulu G. Clinical and pathological studies of an outbreak of Dengue like illness in Visakhapatnam. *Ind J Med Res.* 1965; 53(8):800-12.
- Kalayanarooj S, Vaughn DW, Nimmannitya S, Green S, Suntayakorn S, Kunentrasai N, et al. Early Clinical and Laboratory Indicators of Acute Dengue Illness. *J Infect Dis.* 1997; 176(2):313-21.
- World Health Organization. *Dengue hemorrhagic fever: diagnosis, prevention and control*. 2nd ed. Geneva: WHO; 1997.
- Butt N, Abbassi SM, Munir S, Ahmad M, Sheikh QH. Hematological and Biochemical Indicators for the Early Diagnosis of Dengue

- Viral Infection. *J Coll Physicians Surg Pak*. 2008; 18(5):282–5.
20. Joshi AA, Divyashree BN, Gayathri BR. Hematological Parameters in Dengue: The Serological Angle A Study. *Int J Hematol Res*. 2018; 4(1):180–4.
 21. Tahlan A, Bhattacharya A. Haematological profile of dengue fever. *Int J Res Med Sci*. 2017; 5(12):5367–71.
 22. Khatroth S. A Study on Clinical and Hematological Profile of Dengue Fever in a Tertiary Care Hospital. *IAIM*. 2017; 4(8):96–102.
 23. Yadav SNS. A study of abnormal hematological parameters in dengue fever. *IAIM*. 2018; 5(5):117–20.
 24. Meena KC. A study of hematological profile in dengue fever at tertiary care center. *Int J Adv Med*. 2016; 3(3):621–4.
 25. Qui FX, Gubler DJ, Liu JC, Chen QQ. Dengue in China. A clinical review. *Bull World Health Organ*. 1993; 71(3/4):349–59.
 26. Choudhary BS, Rshiv kumar A, Shankar YA, Manjunatha MM, Priyadarshini. Haematological changes in dengue fever. *Natl J Basic Med Sci*. 2014; 4(4):289–93.
 27. Mohan B, Patwari AK, Anand VK. Hepatic Dysfunction on Childhood Dengue Infection. *J Trop Pediatr*. 2000; 46(1):40–3.
 28. Deshwal R, Qureshi MI, Singh R. Clinical and laboratory profile of dengue fever. *J Associ Physicians India*. 2015; 63:30–2.
 29. Kularatne SA, Gawarammanaib IB, Kumarasiri PR. Epidemiology, clinical features, laboratory investigations and early diagnosis of dengue fever in adults: a descriptive study in Sri Lanka. *Southeast Asian J Trop Med Public Health*. 2005; 36:686–92.
 30. Mandal SK, Gangulyj. Clinical profiles of dengue fever in a teaching hospital of eastern india. *Nat J Med Res*. 2013; 3:173–6.
 31. Arshad I, Hussain A, Malik FA, Shahidaa A, Shah R. Clinicopathologic correlations and their associations with poor outcome. *Professional Med J*. 2011; 18(1):57–63.
 32. Ayub M, Khazinder AM, Lubbad HE, Barlas S, Alfi AY, AI-Ukayli S. Characteristics of Dengue fever in a large public hospital, Jeddah, Saudi Arabia. *J Ayub Med Coll Abbottabad*. 2006; 18(2):9–13.
 33. Chairulfatah A, Setiabudi D, Agoes R, Colebunders R. Thrombocytopenia and Platelet Transfusions in Dengue Haemorrhagic Fever and Dengue Shock Syndrome. *Dengue Bull*. 2003; 27:138–43.
 34. Vaughn DW, Green S, Kalayanarooj S, Innis BL, Nimmannitya S, Suntayakorn S, et al. Dengue viremia titer, antibody response pattern, and virus serotype correlate with disease severity. *J Infect Dis*. 2000; 181(1):2–9.