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## The clinical haematological profile of dengue and the significance of platelet transfusion in its management

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### Abstract

**Background and Objectives:** The objective is to examine the haematological results and establish a connection with the clinical progression, assess the significance of platelet count in forecasting the prognosis in individuals with dengue, and monitor the number of patients who test positive for dengue and require platelet transfusion, as well as the resulting outcome.

**Methods:** A total of 70 individuals who were admitted with fever and tested positive for IgM and/or NS1 were chosen. The study examined a range of haematological, biochemical, and clinical characteristics, as well as the impact of platelet transfusion on the observed outcomes. A comprehensive statistical study was conducted on the different parameters.

**Results:** The study included a total of 70 cases, all of which exhibited fever (100%), headache (100%), myalgia (71%), hepatomegaly (50%), and splenomegaly (43%). 31% of the patients exhibited ascites, whereas 19% showed an increase in haematocrit and pleural effusion. 75% of the cases exhibited leukopenia, while 27% of the cases demonstrated a reversal in the neutrophil lymphocyte ratio. The levels of AST and ALT were elevated, with an average value of 106.08 IU/L and 118.54 IU/L, respectively. In 86% of the instances, platelet transfusion was deemed necessary. On the initial day, transfused platelets accounted for 62% of the cases. 1-2 units of platelets were transfused in 54% of the cases. A total of 58.49% of the patients experienced a recovery period of three days following platelet transfusion.

**Conclusion:** Dengue fever should be strongly suspected when a patient presents with symptoms such as fever, headache, thrombocytopenia, leukopenia, reversal of neutrophil lymphocyte ratio, as well as evidence of capillary leakage including ascites, pleural effusion, and increasing haematocrit. The utilization of platelet transfusion in instances of moderate to severe thrombocytopenia has demonstrated its efficacy in facilitating a successful and seamless recuperation process.

**Keywords:** Dengue, platelet transfusion, thrombocytopenia, leukopenia, IgM

### Introduction

The initial documented outbreaks of dengue fever took place in Asia, Africa, and North America between 1779 and 1780. The simultaneous occurrence of outbreaks in three continents indicates that these viruses and their mosquito vectors have been globally distributed in tropical regions for over two centuries. During this period, DF was seen as a benign and non-lethal illness affecting those visiting tropical regions. Typically, significant temporal gaps ranging from 10 to 40 years were observed between major epidemics, mostly because to the limited ability of viruses and their mosquito vectors to withstand the sluggish transportation required for the emergence of a new serotype within a vulnerable population<sup>[1, 2, 3]</sup>. The dengue pandemic originated in South East Asia following World War II and has since disseminated globally. Subsequently, there has been an increase in the frequency of epidemics caused by many serotypes (known as hyperendemicity). Additionally, the geographical spread of dengue viruses and their mosquito vectors has expanded, leading to the emergence of dengue hemorrhagic fever (DHF) throughout the Americas and the Pacific region. The global epidemiological patterns of dengue fever, also known as dengue hemorrhagic fever, are undergoing rapid transformations<sup>[4, 5]</sup>.

The experience of India in relation to this sickness is both intriguing and captivating. In recent years, there has been a notable alteration in the progression of the disease, resulting in the manifestation of severe cases known as DHF, as well as a rising occurrence of outbreaks. The factors contributing to this resurgence include: Unmatched expansion of the human population, Unintentional and uncontrolled settlement, Inadequate waste management and

water provision, Increased movement and concentration of vector mosquitoes, and Inadequate implementation of mosquito control measures. 6. Escalated advancement and dissemination of the dengue virus. Dengue fever causes changes in hematological parameters such as hemoglobin level, total white blood cell count, differential white blood cell count, and platelet count. The prevailing observations consist of thrombocytopenia accompanied by simultaneous haemoconcentration [5, 6].

The Technical Advisory Committee on Dengue Haemorrhagic fever for South East Asia Western Pacific areas in 1975 and 1980 has revised a guide for the analysis, treatment, and control of Dengue fever. The criteria encompass four primary manifestations, namely: Fever and hemorrhagic manifestations. Hepatomegaly, Propensity to experience shock, two alterations in laboratory parameters Thrombocytopenia and concomitant haemoconcentration have been demonstrated to be effective in detecting and screening for suspicion in 95% of instances. Currently, Dengue has established itself as the preeminent viral disease transmitted by mosquitoes on a global scale. According to current estimates, Dengue is prevalent in at least 112 nations and poses a danger to around 40% of the global population residing in tropical and subtropical regions. Each year, approximately 100 million cases of dengue fever and 500,000 cases of dengue hemorrhagic fever (DHF) occur globally. In order to mitigate disease-related morbidity and mortality, it is crucial to promptly identify and initiate treatment, as well as administer platelet transfusion, in cases where it is needed [7, 8].

## Materials and Methods

A descriptive cross-sectional study was done on a sample of 70 patients at Department of Pathology, Maharajah Institute of Medical Sciences, Vizianagaram, Andhra Pradesh, India from December 2013 to November 2014. The study focused on cases of dengue that were clinically suspected and confirmed through serological investigations using IgM ELISA, with or without NS1 antigen positivity. The researchers examined numerous parameters associated with these cases. The individuals were monitored from the

moment of admission until their recovery or release. The statistical analysis package is used to calculate the mean, standard deviation, and statistical parameters. Appropriate analytical tests are examined [9].

## Inclusion criteria

1. All individuals who test positive for dengue (Dengue IgM antibody, NS1 antigen).
2. The age range is 13 years and older.

## Exclusion criteria

1. Instances of suspected dengue cases where serology results indicate a negative result.
2. Individuals who test positive for dengue fever but also test positive for other concurrent diseases such as malaria and typhoid.
3. Non-consent from patients.

## Result

**Table 1:** Duration of fever in patients

| Fever period | No. of patients | (%)   |
|--------------|-----------------|-------|
| 5 days       | 18              | 26.00 |
| 6 days       | 19              | 27.00 |
| 7 days       | 15              | 21.00 |
| 8 days       | 07              | 10.00 |
| 9 days       | 03              | 4.00  |
| 10 days      | 08              | 11.00 |

**Table 2:** Musculoskeletal complaints in patients

| Musculoskeletal complaints | No. of patients | (%)   |
|----------------------------|-----------------|-------|
| Headache                   | 70              | 100   |
| Retro orbital pain         | 12              | 17.00 |
| Myalgia                    | 50              | 71.00 |
| Arthralgia                 | 10              | 14.00 |

**Table 3:** Serology evaluation in patients

| Serology evaluation           | No. of patients | (%)   |
|-------------------------------|-----------------|-------|
| NS1(Nonstructural protein -1) | 0               | 00.00 |
| IgM (Immunoglobulin M)        | 37              | 53.00 |
| NS1+IgM                       | 33              | 47.00 |

**Table 4:** Peripheral smear estimation in patients

| Peripheral smear estimation           | No. of patients | Percentage (%) |
|---------------------------------------|-----------------|----------------|
| Anemia                                | 09              | 13.00          |
| Leukopenia                            | 06              | 9.00           |
| Thrombocytopenia                      | 19              | 27.00          |
| Leukopenia with Thrombocytopenia      | 22              | 31.00          |
| Anemia with Thrombocytopenia          | 11              | 16.00          |
| Anemia+ Leukopenia + Thrombocytopenia | 10              | 14.00          |

**Table 5:** The categorization of patients based on the duration required to restore platelet count to a normal range

| Days   | No. of patients | Percentage (%) |
|--------|-----------------|----------------|
| 2 days | 06              | 8.5            |
| 3 days | 26              | 37.14          |
| 4 days | 13              | 18.57          |
| 5 days | 06              | 8.57           |
| 6 days | 08              | 11.42          |

**Table 6:** Platelet transfusion Initiation Day in patients

| Platelet transfusion Initiation Day | No. of patients | Percentage (%) |
|-------------------------------------|-----------------|----------------|
| 0 day                               | 06              | 8.5            |
| 1 <sup>st</sup> day                 | 31              | 44.28          |
| 2 <sup>nd</sup> day                 | 13              | 18.57          |
| 3 <sup>rd</sup> day                 | 09              | 12.85          |

## Discussion

The prevalence of dengue fever remains a prominent arboviral infection, resulting in important socioeconomic and healthcare implications. The clinical spectrum comprises a variety of presentations, which include non-specific viral disease, classical dengue fever, life-threatening dengue hemorrhagic fever, and dengue shock syndrome. The basic technique for getting favorable results is the prompt detection and proactive therapy, notably for DHF and DSS. The research investigation centered on a group of 70 individuals who were admitted to our medical facility displaying indications of dengue fever and yielding positive results for NS1/IgM ELISA. The average age of the study group was 36.84 years. Nadeem MA *et al.* did a study that yielded a mean age of 36 years, while Tiwari KN *et al.* conducted a study with a mean age of 34.7 years. The present study involved the examination of a sample size of 70 cases, wherein 29 cases (58%) were classified as males and 21 instances (42%) were classified as females<sup>[10, 11]</sup>. The gender ratio seen in the 556 instances differed from the study conducted by Nadeem MA *et al.*, with 390 (70% men) and 166 (30%) females. Raju BJ *et al.* conducted a study that investigated the gender distribution among a sample of 200 patients. 121 individuals (60.5%) in the entire sample were male. Among the entire population, 79 people (39.5%) were identified as females. The examinations conducted in our study revealed a greater representation of male participants in comparison to the prior research<sup>[12]</sup>.

All subjects in our investigation exhibited signs of fever upon admission. In a similar vein, Turbadkar *et al.*, Mandal *et al.*, Karyawasam *et al.*, Nadeem *et al.*, Tiwari *et al.*, and Raju *et al.* conducted investigations wherein all patients (100%) had symptoms of fever. Fever rates of 99%, 85%, and 80% were reported by Fatima S *et al.*, Lt Col. Banerjee M *et al.*, and Khan AH *et al.*, respectively<sup>[12, 13]</sup>.

The results of our analysis demonstrated a robust link with the bulk of the searches. All patients had headache, with a prevalence incidence of 100%. The reported prevalence of headache was found in previous studies conducted by Raju BJ *et al.* (98%), Lt. Col. Banerjee M *et al.* (63%), Mandal KS *et al.* (62.16%), Khan AH *et al.* (50%), and Turbadkar D *et al.* (13.9%). In contrast to earlier research, the current study did not consider headache to be a significant symptom in the aforementioned examinations. The aforementioned symptom is commonly acknowledged as a distinctive attribute of Dengue disease. In our study, a total of 70 occurrences were examined, with 7 individuals (14%) demonstrating this particular symptom. Raju BJ *et al.* conducted a study including 200 patients of dengue, whereby they observed that 26.5% of the subjects exhibited retroorbital pain. A total of 86% (43 out of 50) of the participants involved in our study exhibited symptoms of myalgia. In a study conducted by Raju BJ *et al.*, it was observed that 85.5% of the patients exhibited symptoms of myalgia. In a similar vein, Lanerjee M *et al.* documented that 81% of patients experienced myalgia, Kariyawasam S *et al.* reported a prevalence of 70%, and Turbadkar D *et al.* reported a prevalence of 25%. The presence of myalgia was found by Tiwari *et al.* in 24% of the patients and Khan *et al.* in 10% of the patients. The occurrence of arthritis was documented in 10% of the subjects. Raju BJ *et al.* reported an incidence rate of 16% among their study group. The study sample consisted of 6 patients (12%) who were diagnosed with upper respiratory tract infection (URTI), and

8 patients (16%) who had a lower respiratory tract infection. Khan AH *et al.*'s investigation revealed that 35% of the cases exhibited symptoms consistent with URTI<sup>[13, 14, 15]</sup>.

Fourteen patients, including 24% of the sample, reported experiencing abdominal pain. Raju *et al.* (year) documented a prevalence rate of 55%, whereas Tiwari *et al.* (year) recorded a prevalence rate of 34% among individuals experiencing abdominal pain. A cohort of 20 participants, constituting 40% of the sample, indicated the presence of symptoms characterized by nausea and vomiting. The incidence rate of 84.5% was reported by Raju *et al.* (58), while Khan *et al.* (60%) and Tiwari *et al.* (36%) reported comparable percentages. A total of 7 patients, or 14% of the overall sample, had symptoms of diarrhea. No instances of diarrhea were observed in any of the additional examinations carried out on the research cohort. A total of 26 patients, or 52% of the whole sample, were found to have hepatomegaly. In their respective patient populations, Raju *et al.* (30%) and Banerjee *et al.* (15%) documented an incidence rate of 15%. A total of 24 patients, or 48% of the overall sample, had splenomegaly. Lieutenant Colonel Banerjee M *et al.* reported that splenomegaly was present in 7% of the patients. DHF and DSS are distinguished by the occurrence of capillary leakage. Two commonly observed signs include a persistent rise in hematocrit levels, the presence of ascites, and the occurrence of pleural effusion. The assessment of pleural effusion was conducted using either chest radiography or ultrasonography monitoring. Pleural effusion was observed in 14% of our patients. Fatima S *et al.* reported an incidence rate of 19% (25 out of 131 cases). Ultrasonographic examination was employed to assess the presence of ascites<sup>[15, 16, 17]</sup>.

Within our study cohort, a total of 13 participants (26%) exhibited the presence of ascites. The prevalence rate of dengue among a cohort of 121 persons who tested positive was observed by Raju BJ *et al.* to be 21.5%. Fatima S *et al.* found that the incidence rate was 11.5% (15 out of 131 cases) in their investigation. Eight patients, representing 16% of the overall sample, exhibited an elevation in haematocrit levels. The incidence rate of 73% was reported by Fatima S *et al.* in their study. Nadeem MA *et al.* conducted a study on dengue patients at two well-known public sector tertiary care institutes in Lahore, Pakistan. They found that 21% of the 390 patients saw an elevation in haematocrit levels. The identification of dengue fever was confirmed by employing NS1 ELISA and IgM ELISA assays, incorporating those who had positive IgM results<sup>[18, 19]</sup>.

Out of a total of 50 patients, 29 individuals (58%) exhibited a positive result only for IgM, whereas the remaining 21 individuals (42%) displayed positive results for both NS1 and IgM. Bandyopadhyay B *et al.* did a study at Calcutta School of Tropical Medicine, wherein they investigated patients exhibiting symptoms of DF by the utilization of the NS1 and IgM ELISA assays. The research encompassed a cohort of 64 individuals, out of which 38 exhibited positive results for NS1. Out of the total sample size of 38 patients, 24 individuals exhibited a positive result on the IgM test, whilst the other 14 cases tested negative for IgM ELISA. The occurrence of secondary dengue infection can be attributed to the likely occurrence of undetectable levels of IgM antibodies. Fatima S *et al.* did a study wherein they employed IgM, IgG ELISA, and NS1 ELISA assays to screen people displaying signs of dengue fever. There were 131 cases that tested positive for dengue fever. Out of the

entire cohort of 131 patients, 35 people (27%) exhibited a positive result exclusively for IgM, whereas 63 patients (48%) demonstrated positive results for both IgM and NS1. Turbadkar *et al.* did a study where they tested a group of 3,677 patients who showed symptoms of DF using IgM and IgG ELISA testing. A total of 503 patients tested positive for the serological markers, as indicated by the results [20, 21]. Out of the entire sample, 288 persons (57.25%) exhibited positive results for IgM ELISA alone, whereas 108 instances (21.4%) demonstrated positive results for IgG ELISA alone, and 107 cases (21.4%) exhibited positive results for both IgM and IgG ELISA. The current investigation documented an occurrence rate of 8% within a cohort of four individuals, whereas the research conducted by Banerjee *et al.* (year) documented an occurrence rate of 11% within a cohort of fifty individuals. A total of 22 patients, representing 44% of the overall sample, had leukopenia. Conversely, the research carried out by Lin SF *et al.* revealed a greater occurrence of leucopenia in individuals diagnosed with dengue fever, totaling 76%. Banerjee *et al.* (year) conducted a study whereby they noticed that leukopenia was not observed in any of the 50 cases of DF. A total of 48 instances (96%) exhibited thrombocytopenia in our investigation, as indicated by the grading system. Among all the cases examined, it was observed that 12 cases (25%) had grade 1 thrombocytopenia, 5 instances (10.42%) exhibited grade 2, and 22 cases (45.83%) displayed Grade 3 and Grade 4 (54.83%). Turbadkar *et al.* conducted a study including a sample size of 212 patients, whereby it was shown that 76.74% of the participants exhibited thrombocytopenia. Sarwat Fatima *et al.* conducted a study wherein they observed that 89% of the 131 participants who tested positive for thrombocytopenia. Kariyawasam *et al.* (year) conducted a study whereby they observed that all 15 pregnant patients who tested positive for DF exhibited a complete occurrence of thrombocytopenia [22, 23].

The prevalence rate of thrombocytopenia among a sample of 556 individuals who tested positive for dengue fever during the 2011 epidemic in Lahore, Pakistan was established as 93% by Nadeem MA *et al.* (year) in their study. Khan MU *et al.* found that 67.2% of the 210 people who tested positive for dengue had thrombocytopenia. Khan *et al.* observed a prevalence rate of 71% for thrombocytopenia.

Our analysis revealed that 12 patients, or 24% of the overall sample, had hyperbilirubinemia, primarily caused by S. bilirubin. No description of jaundice in the aforementioned patients has been provided in any of the listed research studies. A considerable proportion of our patient population encountered transaminitis. 78% (39 cases) of our patients exhibited elevated SGOT levels, while 76% (38 cases) showed high SGPT levels. Mandal SK *et al.* conducted a study in which they reported a prevalence rate of transaminitis at 83.83%. In their study, Kariyawasam *et al.* (year) observed a comprehensive manifestation of elevated liver enzymes (SGOT, SGPT) in a cohort of 15 pregnant women who tested positive for these enzymes. In our investigation, the mean SGOT (AST) levels were determined to be 141.60 IU/L. The SGPT (ALT) levels were determined to be 118.54 IU/L. Prakash O *et al.* conducted a study involving 699 seropositive cases to comprehensively investigate hepatitis in dengue fever at a tertiary care hospital in Karachi, Pakistan. The mean serum glutathione (SGOT (AST)) level was reported by the researchers as 174 IU/L, while the serum glutathione (SGPT (ALT)) level was found to be 88.50 IU/L. The prothrombin time INR (PT-

INR) typically falls within the range of 0.8 to 1.2. The findings of our study indicate that a proportion of 14% of the patients demonstrated an extended prothrombin time. An extended activated partial thromboplastin time (aPTT) was observed in 10 patients, representing 20% of the sample. None of the examinations revealed any significant abnormalities in the coagulation profile. Serum urea and creatinine levels: A limited number of our patients have exhibited mild renal failure, with all of them thereafter achieving complete restoration of renal function either at release or over the follow-up period. Out of the total number of patients, 10 individuals (20%) had higher blood urea levels, while 9 individuals (18%) had increased serum creatinine levels. The stated research does not offer conclusive facts regarding this issue [23].

Within our study cohort, a total of 43 participants, accounting for 86% of the sample, had platelet transfusion. The indication is limited to cases of moderate to severe thrombocytopenia. Tiwari KN *et al.* did a retrospective analysis which revealed that thrombocytopenia was the predominant indication for platelet transfusion in four tertiary care institutions situated in Delhi. The study comprised a cohort of 230 patients who tested positive for the serotype, out of which 130 cases (56.5%) experienced platelet transfusion. Thrombocytopenia was the predominant indication, rather than the manifestation of bleeding. According to Kulkarni's research, a total of 118 individuals out of a sample size of 232, who had platelet counts ranging from 20,000 to 1.00.000 cells/cu.mm, underwent a single unit platelet transfusion. Furthermore, it was observed that 64 patients, accounting for 27.5% of the total, who had platelet counts below 20,000 cells/cu.mm, underwent several platelet transfusions. The research findings indicated that a majority of platelet transfusions, specifically 51%, were considered inappropriate. Furthermore, it was seen that delivering the transfusion with a platelet count of 20,000 yielded superior efficacy.

Out of the total sample size of 50 cases, 29 individuals (58%) were identified as having dengue fever, whereas 21 individuals (42%) were diagnosed with dengue hemorrhagic fever (DHF) [23, 24].

None of the patients in our research group exhibited DSS. In the study conducted by Fatima S *et al.*, it was shown that of the 131 instances of dengue that yielded positive results, 60% exhibited DF, 35.5% displayed DHF, and 4.5% had DSS. Arif M *et al.* did a study whereby they examined 556 instances of seropositive dengue. The findings revealed that 439 cases (78%) exhibited DF, 95 cases (17%) displayed DHF, and 26 cases (4%) displayed DSS. Khan *et al.* conducted a study at a teaching hospital located in rural Melmaruvathur, Tamil Nadu, where they evaluated a cohort of 107 persons who tested positive for serotypes. Out of the total cases examined, 58 (54.2%) exhibited DF, 38 (35.5%) displayed DHF, and 11 (10.2%) displayed DSS. Hati AK *et al.* conducted a study in West Bengal and discovered that 90% of patients exhibited DF, whereas 10% had DHF. A seropositive population of 230 patients was detected in a study conducted by Tiwari KN *et al.* in Delhi. Out of the whole sample size, 163 people (70.8%) showed DF, while 29.2% showed DHF [24].

## Conclusion

Dengue has emerged as a global arboviral ailment, characterized by a rising incidence of epidemics and a heightened manifestation of severe symptoms, notably Dengue Haemorrhagic Fever, particularly in tropical and

subtropical areas. The potential for the dissemination of this illness to temperate regions is increasing as a result of climate change and global warming. Our study aimed to investigate the hematological features of dengue fever and their correlation with the clinical advancement. The findings of the study imply that the presence of fever and headache, along with thrombocytopenia, leukopenia, and a reversal of neutrophil lymphocyte ratio, provides compelling evidence for the diagnosis of Dengue fever. Hence, it is imperative to conduct screening and verification procedures for this particular diagnosis.

The presence of capillary leakage indicators, such as a rising haematocrit, ascites, and pleural effusion, should be regarded as a crucial alert to healthcare providers, prompting them to swiftly and assertively address the heightened susceptibility to Dengue Haemorrhagic Fever. Significant prognostic markers during the period of hospitalization and subsequent surveillance were identified as thrombocytopenia and a 20% increase in haematocrit (PCV) from the first test. The study also investigated the commencement of platelet transfusion in patients with varying degrees of thrombocytopenia, ranging from mild to severe. The patients underwent a smooth and rapid recovery without any adverse effects linked to the transfusion. All patients in our study group who exhibited anomalies in clinical, haematological, and biochemical markers, either during their hospitalization or during the ensuing follow-up period, demonstrated full recovery. In conclusion, the prompt detection, assessment, diagnosis, and prompt intervention of Dengue fever will substantially diminish the incidence of morbidity and mortality linked to this alarming ailment.

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#### Conflict of interest

None.

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