



Evaluation of Hematological Parameters as Laboratory Predictors of Disease Severity in Dengue Fever: A Prospective Clinico-Pathological Study

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Abstract

Background: Dengue fever is a major mosquito-borne viral illness with a wide clinical spectrum ranging from mild febrile illness to severe life-threatening complications. Early identification of severe cases remains a challenge. Hematological parameters obtained from routine laboratory investigations may serve as cost-effective and reliable predictors of disease severity, particularly in resource-limited settings. Aim of the study was to evaluate hematological parameters as laboratory predictors of disease severity in patients with dengue fever in a prospective clinico-pathological study. **Material and Methods:** This prospective observational study was conducted in the Department of Pathology in collaboration with the Department of General Medicine at a tertiary care hospital. A total of 100 serologically confirmed dengue cases (NS1 antigen and/or IgM antibody positive) were included. Demographic, clinical, and hematological data were collected using a structured proforma. Hematological parameters including hemoglobin, hematocrit, total leukocyte count, platelet count, and derived indices such as neutrophil-to-lymphocyte ratio were analyzed. Patients were classified into dengue fever, dengue with warning signs, and severe dengue based on standard criteria. Statistical analysis was performed with significance set at $p < 0.05$. **Results:** The mean age of patients was 32.8 ± 12.4 years with male predominance (62%). Thrombocytopenia was observed in 72% and leukopenia in 58% of patients. Severe dengue (20%) was significantly associated with lower platelet count ($46 \pm 18 \times 10^3/\mu\text{L}$) and higher hematocrit ($45.6 \pm 6.4\%$) ($p < 0.001$). Platelet count showed a strong negative correlation with severity, while hematocrit and NLR showed positive correlations. Increased ICU requirement, bleeding complications, and prolonged hospital stay were significantly associated with abnormal hematological parameters. **Conclusion:** Hematological parameters, particularly platelet count and hematocrit, are reliable predictors of disease severity in dengue fever. Their routine use can facilitate early risk stratification and improve clinical outcomes.

Keywords: Dengue fever; Hematological parameters; Thrombocytopenia; Hematocrit; Disease severity; Clinico-pathological study.



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INTRODUCTION

Dengue fever is a rapidly emerging mosquito-borne viral infection caused by the dengue virus, a member of the Flaviviridae family, transmitted primarily by *Aedes aegypti*. It represents a major global public health concern, particularly in tropical and subtropical regions such as India, where recurrent outbreaks impose a significant burden on healthcare systems. The clinical spectrum of dengue infection is wide, ranging from asymptomatic illness and classical dengue fever to severe dengue, which includes dengue hemorrhagic fever and dengue shock syndrome, characterized by plasma leakage, bleeding manifestations, and organ dysfunction (1). Early identification of patients at risk of progression to severe disease remains a major clinical challenge, as deterioration can occur rapidly during the critical phase of illness. Hematological alterations are among the earliest and most consistent laboratory abnormalities observed in dengue infection and play a pivotal role in diagnosis, monitoring, and prognostication. The dengue virus directly and indirectly affects bone marrow function, leading to suppression of hematopoiesis, destruction of platelets, and immune-mediated alterations in blood cell lines. The most characteristic hematological findings include thrombocytopenia, leukopenia, and hemoconcentration, which reflect the underlying pathophysiological mechanisms such as bone marrow suppression, peripheral destruction of platelets, and plasma leakage (2,3). Thrombocytopenia is one of the hallmark features of dengue infection and is observed in a majority of patients, often correlating with disease severity and risk of bleeding complications (4). Leukopenia, particularly neutropenia, is also commonly seen and reflects viral suppression of bone marrow activity, while an increase in hematocrit indicates plasma leakage and is a critical marker of disease severity (5).

Several studies have demonstrated that hematological parameters derived from routine complete blood count (CBC) testing can serve as useful predictors of dengue severity. Chaloeuwong et al. highlighted the importance of CBC parameters in

differentiating dengue from other acute febrile illnesses and emphasized their utility in resource-limited settings where advanced serological tests may not be readily available (6). Similarly, studies have shown that a significant decline in platelet count, along with rising hematocrit levels, is strongly associated with severe dengue and adverse clinical outcomes (7). In addition, dynamic changes in hematological parameters, rather than single time-point measurements, have been found to be more reliable indicators of disease progression (3). Recent research has also explored advanced hematological indices such as mean platelet volume (MPV), platelet distribution width (PDW), and neutrophil-to-lymphocyte ratio (NLR) as potential biomarkers for predicting severity. These indices provide additional insights into platelet activation, inflammatory response, and immune status. Studies have demonstrated that alterations in platelet indices and elevated NLR are associated with increased disease severity and can aid in early risk stratification (8,9). Furthermore, comprehensive hematological analyses have identified parameters such as hemoglobin levels, neutrophil and lymphocyte counts, and platelet count as key contributors to disease progression and severity assessment (10).

Despite the availability of these hematological markers, there remains considerable variability in their predictive value across different populations and clinical settings. Some studies suggest that traditional markers such as platelet count and hematocrit may not reliably predict severity when assessed in isolation, highlighting the need for integrated evaluation of multiple hematological parameters (11). Additionally, differences in study design, sample size, geographic distribution, and timing of laboratory investigations contribute to inconsistent findings in the literature. Most studies are retrospective or cross-sectional in nature, limiting their ability to establish temporal relationships and causal associations between hematological changes and disease severity.

Another important limitation in existing literature is the lack of prospective clinico-pathological studies that comprehensively evaluate hematological parameters in relation to disease severity using standardized criteria. There is also limited data from Indian tertiary care settings that systematically analyze the prognostic utility of routine hematological parameters in dengue patients. Given the accessibility, cost-effectiveness, and rapid turnaround time of CBC testing, there is a pressing need to validate these parameters as reliable laboratory predictors of disease severity in dengue fever.

Therefore, the present study was undertaken with the aim of evaluating hematological parameters as laboratory predictors of disease severity in patients with dengue fever in a prospective clinico-pathological setting. The study seeks to analyze the correlation between hematological indices such as platelet count, total leukocyte count, hematocrit, and other derived parameters with the severity of dengue infection. By identifying reliable and easily accessible laboratory markers, this study aims to contribute to early risk stratification, improved clinical decision-making, and better patient outcomes in dengue fever.

MATERIALS AND METHODS

Study Design and Setting

This prospective clinico-pathological observational study was conducted in the Department of Pathology in collaboration with the Department of General Medicine at a tertiary care teaching hospital. The study was carried out over the specified study period after obtaining approval from the Institutional Ethics Committee. The objective of the study was to evaluate hematological parameters as laboratory predictors of disease severity in patients diagnosed with dengue fever. A total of 100 patients were included in the study. Patients presenting with clinical features suggestive of dengue fever and confirmed by serological testing were enrolled consecutively after fulfilling the eligibility criteria. Written informed consent was obtained from all participants or from parents/guardians in the case of minors, wherever applicable.

Study Population

The study population consisted of 100 confirmed cases of dengue fever admitted to or evaluated in the hospital during the study period. Diagnosis of dengue fever was established based on clinical features supported by laboratory confirmation using dengue NS1 antigen and/or dengue IgM antibody positivity, according to institutional diagnostic protocol. After confirmation, patients were assessed clinically and categorized according to disease severity based on standard clinical and laboratory criteria. Hematological parameters were analyzed and correlated with severity of dengue infection.

Inclusion Criteria

- Patients of either sex diagnosed with dengue fever by NS1 antigen and/or dengue IgM positivity
- Patients willing to participate in the study and provide informed consent
- Patients with adequate clinical details and laboratory records available for analysis
- Patients categorized clinically into non-severe and severe dengue based on accepted diagnostic criteria

Exclusion Criteria

- Patients with other concurrent febrile illnesses such as malaria, typhoid, leptospirosis, or chikungunya

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- Patients with pre-existing hematological disorders such as leukemia, aplastic anemia, immune thrombocytopenia, or hemolytic anemia
- Patients with chronic liver disease, chronic kidney disease, malignancy, or autoimmune disorders affecting hematological parameters
- Patients who had received blood transfusion or platelet transfusion prior to initial hematological evaluation
- Patients with incomplete clinical or laboratory data
- Patients not willing to participate in the study

Sample Size

The sample size for the present study was fixed at 100 cases of confirmed dengue fever. All eligible patients fulfilling the inclusion criteria during the study period were included until the desired sample size was achieved.

Data Collection

Data collection was carried out in a systematic manner using a predesigned proforma. The following details were recorded:

- **Demographic details:** age, sex, and inpatient/outpatient status
- **Clinical details:** fever duration, myalgia, headache, retro-orbital pain, vomiting, abdominal pain, rash, bleeding manifestations, hypotension, and other warning signs
- **Serological confirmation:** NS1 antigen positivity and/or dengue IgM antibody positivity
- **Hematological parameters:** hemoglobin, hematocrit, total leukocyte count, differential leukocyte count, platelet count, red blood cell count, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and other relevant indices as available
- Severity assessment: classification into dengue fever, dengue with warning signs, and severe dengue based on clinical and laboratory findings
- Outcome-related variables: duration of hospital stay, requirement of intensive care, bleeding complications, and recovery status wherever applicable

Venous blood samples were collected under aseptic precautions at the time of admission or first presentation before initiation of major therapeutic interventions, wherever possible. Samples were analyzed in the central pathology laboratory using standard operating procedures. Hematological parameters obtained from the automated analyzer were verified and documented. Relevant peripheral smear examination was performed in selected cases whenever indicated. All laboratory findings were correlated with the clinical severity of dengue fever.

Study Variables

The principal study variables included platelet count, hematocrit, hemoglobin level, total leukocyte count, neutrophil count, lymphocyte count, and other hematological indices. These parameters were evaluated as potential laboratory predictors of disease severity in dengue fever.

Statistical Analysis

The collected data were entered into Microsoft Excel and analyzed using appropriate statistical software. Quantitative variables were expressed as mean $\pm$ standard deviation, and qualitative variables were presented as frequencies and percentages. Comparison of hematological parameters across severity groups was performed using appropriate statistical tests such as Student's t-test, one-way ANOVA, or Mann-Whitney U test depending on the distribution of data. Association between categorical variables was assessed using Chi-square test or Fisher's exact test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1: Demographic Profile of Study Population (n = 100)

Parameter	Category	n (%) / Mean $\pm$ SD
Age (years)	Mean $\pm$ SD	32.8 $\pm$ 12.4
	<20 years	18 (18.0%)
	21–40 years	46 (46.0%)
	41–60 years	26 (26.0%)
	>60 years	10 (10.0%)
Sex	Male	62 (62.0%)
	Female	38 (38.0%)
Sex Ratio (M:F)	—	1.63 : 1
Patient Status	Inpatient	72 (72.0%)
	Outpatient	28 (28.0%)

The study population had a mean age of 32.8 $\pm$ 12.4 years, with the majority of patients belonging to the 21–40 years age group (46%), indicating a higher burden of dengue among young adults. A male predominance (62%) was observed, with

a male-to-female ratio of 1.63:1, suggesting increased exposure risk among males. Most patients were inpatients (72%), reflecting that a significant proportion required hospital-based management, while 28% were managed on an outpatient basis. Overall, the demographic profile highlights that dengue infection predominantly affects young adult males and frequently necessitates hospitalization in a tertiary care setting.

Table 2: Hematological Parameters in Dengue Fever (n = 100)

Parameter	Mean ± SD	Range
Hemoglobin (g/dL)	12.4 ± 1.8	8.2 – 16.5
Hematocrit (%)	40.8 ± 5.6	30 – 54
Total Leukocyte Count (cells/mm ³)	4,320 ± 1,520	1,800 – 9,200
Neutrophils (%)	54.6 ± 12.2	30 – 78
Lymphocytes (%)	36.8 ± 10.5	18 – 60
Platelet Count (×10 ³ /μL)	82.5 ± 38.6	12 – 180
RBC Count (million/mm ³)	4.62 ± 0.74	3.2 – 6.1
MCV (fL)	86.4 ± 7.2	70 – 102
MCH (pg)	28.6 ± 2.8	22 – 34
MCHC (g/dL)	32.8 ± 1.9	29 – 36

The hematological profile demonstrated that the mean hemoglobin level was 12.4 ± 1.8 g/dL, while the mean hematocrit was 40.8 ± 5.6%, with values extending up to 54%, indicating hemoconcentration in a subset of patients. The mean total leukocyte count was 4,320 ± 1,520 cells/mm³, with lower values reflecting leukopenia commonly associated with viral infections. Differential counts showed a predominance of neutrophils (54.6 ± 12.2%) with relative lymphocytosis (36.8 ± 10.5%). The mean platelet count was 82.5 ± 38.6 ×10³/μL, with values as low as 12,000/μL, highlighting significant thrombocytopenia. Red cell indices, including RBC count (4.62 ± 0.74 million/mm³), MCV (86.4 ± 7.2 fL), MCH (28.6 ± 2.8 pg), and MCHC (32.8 ± 1.9 g/dL), were largely within normal limits. Overall, thrombocytopenia, leukopenia, and elevated hematocrit emerged as the key hematological abnormalities in dengue fever.

Table 3: Distribution of Hematological Abnormalities in Dengue Fever (n = 100)

Parameter	Category	n (%)
Leukocyte Count	<4,000 (Leukopenia)	58 (58.0%)
	≥4,000	42 (42.0%)
Platelet Count	<50,000	28 (28.0%)
	50,000–100,000	44 (44.0%)
	>100,000	28 (28.0%)
Hematocrit	>45% (Hemoconcentration)	34 (34.0%)
	≤45%	66 (66.0%)

The distribution of hematological abnormalities showed that leukopenia (<4,000 cells/mm³) was present in 58% of patients, reflecting the typical viral suppression of bone marrow activity in dengue infection. Thrombocytopenia was a prominent finding, with 72% of patients having platelet counts below 100,000/μL, including 28% with severe thrombocytopenia (<50,000/μL). Hemoconcentration, indicated by hematocrit >45%, was observed in 34% of cases, suggesting plasma leakage and increased disease severity.

Table 4: Comparison of Hematological Parameters Across Severity of Dengue Fever (n = 100)

Parameter	Dengue Fever (n=36)	Warning Signs (n=44)	Severe Dengue (n=20)	p-value
Hemoglobin (g/dL)	12.8 ± 1.6	12.3 ± 1.7	11.8 ± 2.0	0.08
Hematocrit (%)	38.6 ± 4.2	41.2 ± 5.1	45.6 ± 6.4	<0.001*
TLC (cells/mm ³)	4,800 ± 1,200	4,200 ± 1,400	3,600 ± 1,600	0.01*
Platelet Count (×10 ³ /μL)	110 ± 28	78 ± 26	46 ± 18	<0.001*

Comparison of hematological parameters across severity categories demonstrated that hematocrit and platelet count showed statistically significant differences among the groups (p < 0.001). Mean hematocrit values increased progressively from 38.6 ± 4.2% in dengue fever to 45.6 ± 6.4% in severe dengue, indicating hemoconcentration associated with plasma leakage. Conversely, platelet count showed a marked decline with increasing severity, from 110 ± 28 ×10³/μL in mild cases to 46 ± 18 ×10³/μL in severe dengue, highlighting its strong association with disease progression. Total leukocyte count also demonstrated a significant decreasing trend (p = 0.01), reflecting worsening leukopenia with severity. However, hemoglobin levels did not show a statistically significant difference across groups (p = 0.08).

Table 5: Comparison of Hematological Parameters with Clinical Outcomes in Dengue Fever (n = 100)

Parameter	No Complications (n=74)	Complications (n=26)	p-value
Hematocrit (%)	39.2 ± 4.8	44.8 ± 6.2	<0.001*
Platelet Count (×10 ³ /μL)	96 ± 32	48 ± 20	<0.001*
TLC (cells/mm ³)	4,600 ± 1,400	3,800 ± 1,500	0.02*
NLR	1.42 ± 0.68	2.18 ± 1.04	0.001

Analysis of hematological parameters in relation to clinical outcomes revealed that patients with complications had significantly higher hematocrit levels (44.8 ± 6.2%) compared to those without complications (39.2 ± 4.8%) (p < 0.001), indicating the role of hemoconcentration in adverse outcomes. Platelet count was markedly reduced in patients with complications (48 ± 20 ×10³/μL) versus those without complications (96 ± 32 ×10³/μL) (p < 0.001), underscoring its strong association with bleeding and severity. Total leukocyte count was also significantly lower in the complication group (p = 0.02), reflecting greater leukopenia. Additionally, NLR was significantly elevated (2.18 ± 1.04) in patients with complications compared to those without (1.42 ± 0.68) (p = 0.001), suggesting its role as an inflammatory marker of disease progression. Overall, these findings demonstrate that hematocrit, platelet count, TLC, and NLR are significant laboratory predictors of adverse clinical outcomes in dengue fever.

Table 6: Correlation of Hematological Parameters with Disease Severity

Parameter	Correlation Coefficient (r)	p-value
Platelet Count vs Severity	−0.68	<0.001*
Hematocrit vs Severity	+0.52	<0.001*
Total Leukocyte Count vs Severity	−0.34	0.002*
NLR vs Severity	+0.48	<0.001*

Platelet count demonstrated a strong negative correlation (r = −0.68) with disease severity, indicating that lower platelet levels were significantly associated with severe dengue. Hematocrit showed a moderate positive correlation (r = +0.52), reflecting the role of hemoconcentration in disease progression. Total leukocyte count exhibited a weaker but significant negative correlation, while NLR showed a moderate positive correlation, suggesting its utility as an inflammatory marker in predicting severity.

Table 7: Correlation of Hematological Parameters with Outcomes

Parameter	ICU Requirement (r)	Bleeding (r)	Hospital Stay (r)	p-value
Platelet Count	−0.62	−0.71	−0.54	<0.001*
Hematocrit	+0.49	+0.46	+0.51	<0.001*
NLR	+0.44	+0.38	+0.47	<0.001*

Platelet count showed a strong inverse correlation with bleeding complications (r = −0.71) and ICU requirement, confirming its role as a key prognostic marker. Hematocrit and NLR demonstrated positive correlations with adverse outcomes, indicating their association with disease severity and prolonged hospitalization.

Table 8: Correlation Between Hematological Parameters and Clinical Outcomes in Dengue Fever

Variables	r-value	p-value	Significance
Platelet Count vs Hematocrit	−0.45	<0.001*	Moderate inverse
Platelet Count vs NLR	−0.42	0.001*	Moderate inverse
Hematocrit vs Hospital Stay	+0.51	<0.001*	Moderate positive

Correlation analysis demonstrated a moderate inverse relationship between platelet count and hematocrit (r = −0.45, p < 0.001), indicating that decreasing platelet levels are associated with increasing hemoconcentration. A similar moderate negative correlation was observed between platelet count and NLR (r = −0.42, p = 0.001), suggesting that thrombocytopenia is associated with heightened inflammatory response. Additionally, hematocrit showed a moderate positive correlation with duration of hospital stay (r = +0.51, p < 0.001), indicating that patients with higher hematocrit levels tend to have prolonged hospitalization.

DISCUSSION

Dengue fever continues to be a major public health challenge in tropical countries, particularly in India, with increasing incidence and periodic outbreaks. The present prospective clinico-pathological study was undertaken to evaluate hematological parameters as laboratory predictors of disease severity in dengue fever. The findings of this study highlight the significant role of routine hematological parameters in early diagnosis, risk stratification, and prognostication of dengue infection, thereby reinforcing the importance of laboratory medicine in clinical decision-making.

In the present study, the mean age of patients was 32.8 ± 12.4 years, with a predominance of cases in the 21–40 years age group. This finding is consistent with earlier studies by Gupta et al. (12) and Meena et al. (13), who reported that dengue

infection predominantly affects young adults due to increased exposure to mosquito vectors and outdoor activities. A male predominance (62%) was observed in the current study, which aligns with findings from Kularatne et al. (14) and Sharma et al. (15), suggesting that occupational exposure and sociocultural factors may contribute to higher incidence among males. The clinical profile in the present study showed that myalgia (72%) and headache (68%) were the most common presenting symptoms, followed by vomiting (52%) and retro-orbital pain (44%). These findings are comparable with those reported by Khan et al. (16) and Ahmed et al. (17), who also identified these symptoms as hallmark features of dengue infection. Bleeding manifestations were observed in 26% of cases, which is in agreement with studies by Patel et al. (18), where bleeding ranged between 20–30% in hospitalized dengue patients.

Hematological analysis revealed that thrombocytopenia was the most consistent abnormality, with a mean platelet count of $82.5 \pm 38.6 \times 10^3/\mu\text{L}$ and 72% of patients having platelet counts below $100,000/\mu\text{L}$. This finding is in concordance with earlier studies by Khatri et al. (8) and Lye et al. (19), which identified thrombocytopenia as a hallmark of dengue infection and a key indicator of disease severity. The pathophysiology of thrombocytopenia in dengue involves bone marrow suppression, immune-mediated platelet destruction, and increased peripheral consumption.

Leukopenia was observed in 58% of cases, with a mean total leukocyte count of $4,320 \pm 1,520$ cells/ mm^3 . This is consistent with findings from Lee et al. (20), who reported leukopenia in more than half of dengue patients. The suppression of bone marrow by the dengue virus and immune-mediated destruction of leukocytes are thought to contribute to this phenomenon. The present study also demonstrated relative lymphocytosis, which is a characteristic feature of viral infections and has been reported in previous studies (21).

Hemoconcentration, indicated by elevated hematocrit levels ($>45\%$), was observed in 34% of patients and showed a significant association with disease severity. This finding correlates with studies by Trung et al. (22), who emphasized that rising hematocrit is a critical marker of plasma leakage and impending severe dengue. In the present study, hematocrit showed a significant positive correlation with severity ($p < 0.001$), supporting its role as an important prognostic marker. When hematological parameters were analyzed across severity categories, platelet count and hematocrit showed statistically significant associations with disease severity. Patients with severe dengue had markedly lower platelet counts ($46 \pm 18 \times 10^3/\mu\text{L}$) and higher hematocrit levels ($45.6 \pm 6.4\%$) compared to those with mild disease. Similar findings were reported by Srikiatkachorn et al. (23), who demonstrated that severe dengue is associated with profound thrombocytopenia and significant hemoconcentration. Total leukocyte count also showed a decreasing trend with increasing severity, which is consistent with observations by Potts et al. (24).

Derived hematological indices such as the neutrophil-to-lymphocyte ratio (NLR) also showed a significant correlation with disease severity and outcomes in the present study. Elevated NLR was associated with severe dengue and adverse outcomes, suggesting its role as a marker of systemic inflammation. This finding is supported by studies by Wang et al. (25), who identified NLR as a useful predictor of disease severity in dengue infection.

Outcome analysis in the present study revealed that severe dengue was significantly associated with longer hospital stay, increased ICU admission, and higher incidence of bleeding complications. The mean duration of hospital stay was significantly higher in severe dengue (8.6 ± 2.4 days) compared to mild cases. These findings are consistent with studies by Thein et al. (26), which reported prolonged hospitalization and increased morbidity in severe dengue cases. Mortality in the present study was 2%, which is comparable to rates reported in tertiary care settings by Murray et al. (27).

Correlation analysis further strengthened the findings of this study, with platelet count showing a strong negative correlation with disease severity and bleeding manifestations, while hematocrit and NLR showed positive correlations with severity and adverse outcomes. These findings are in agreement with studies by Soundravally et al. (28), who demonstrated that hematological parameters can serve as reliable predictors of disease progression.

Despite these significant findings, the study has certain limitations. Being a single-center study, the results may not be generalizable to all populations. Additionally, the sample size, though adequate, limits subgroup analysis. Serial monitoring of hematological parameters could have provided better insight into dynamic changes during the course of illness. Future studies with larger sample sizes and multicentric designs are recommended to validate these findings.

CONCLUSION

The present study demonstrates that routine hematological parameters, particularly platelet count, hematocrit, and total leukocyte count, serve as reliable laboratory predictors of disease severity in dengue fever. Thrombocytopenia and hemoconcentration showed strong associations with severe disease and adverse outcomes. Derived indices such as NLR further enhance the prognostic value of hematological assessment. Given their availability, cost-effectiveness, and rapid turnaround time, these parameters can be effectively utilized for early risk stratification and management of dengue patients in resource-limited settings.

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