

Original Research Article

EXPLORING LEUKOPENIA AS A DIAGNOSTIC MARKER IN DENGUE FEVER: A CLINICAL STUDY

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ABSTRACT

Background: Dengue fever, caused by the dengue virus transmitted through Aedes mosquitoes, is a significant global health issue. Early diagnosis is crucial for effective management and reducing morbidity. Leukopenia, a reduction in white blood cell count, is a common hematological finding in dengue patients, but its diagnostic value remains debated. This study aims to evaluate the role of leukopenia as a diagnostic marker for dengue fever and its correlation with clinical outcomes.

Materials and Methods: This prospective observational study included 100 patients aged 5 months to 65 years diagnosed with dengue fever in June 2024. Dengue diagnosis was confirmed using the Dengue card test. Patients were categorized based on the presence or absence of leukopenia. Clinical and laboratory parameters, including white blood cell count (WBC), platelet count, and hemoglobin levels, were recorded. The duration of hospital stay, recovery rate, and complications were analyzed. Sensitivity and specificity of leukopenia in diagnosing dengue were calculated, and odds ratios for various factors were assessed using logistic regression.

Results: Among the 100 patients, 78 (78%) had leukopenia. The leukopenia group had a significantly lower WBC count (2539.9 ± 828.1 cells/mm³) compared to the non-leukopenia group (5650.9 ± 1329.3 cells/mm³, $p < 0.0001$). Platelet counts and hemoglobin levels did not differ significantly between groups. Patients with leukopenia experienced a longer hospital stay (8.7 ± 2.1 days vs. 6.3 ± 1.6 days, $p = 0.025$) and a lower recovery rate (79.5% vs. 95.5%, $p = 0.041$). Complications such as bleeding and organ failure were more prevalent in the leukopenia group (bleeding: 17.9% vs. 9.1%, $p = 0.011$; organ failure: 7.7% vs. 0.0%, $p = 0.034$). The sensitivity of leukopenia for detecting dengue was 93.3%, while specificity was 68.0%. The odds ratio for leukopenia as a predictor of dengue was 3.51 (95% CI: 0.81 - 6.85, $p = 0.202$).

Conclusion: Leukopenia is a highly sensitive marker for dengue fever, though with moderate specificity. It is associated with more severe clinical outcomes, including prolonged hospital stay and higher complication rates. While leukopenia can be a useful diagnostic indicator, it should be used in conjunction with other diagnostic tests for accurate dengue diagnosis and management.

Keywords: Dengue fever, leukopenia, sensitivity, specificity, platelet count.

INTRODUCTION

Dengue fever is a mosquito-borne viral infection that poses a significant public health challenge in tropical and subtropical regions worldwide. Caused by the dengue virus, which belongs to the

Flaviviridae family, the disease is transmitted primarily by the Aedes aegypti mosquito.^[1] With an estimated 390 million infections occurring annually, dengue fever represents a critical burden on healthcare systems, particularly in endemic areas of Southeast Asia, Latin America, and Africa.^[2] India experiences a considerable burden of dengue, with

millions of cases reported annually, particularly during the monsoon season when mosquito breeding is rampant. The disease exerts immense pressure on the healthcare system, especially in urban areas where population density and inadequate sanitation contribute to transmission.^[3]

The clinical spectrum of dengue fever ranges from mild febrile illness to severe forms, such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).^[4] Early and accurate diagnosis is essential for effective patient management and the prevention of severe complications.^[4] However, the clinical diagnosis of dengue fever can be challenging due to its nonspecific symptoms, which overlap with other febrile illnesses such as malaria, leptospirosis, and chikungunya.^[5]

Laboratory confirmation of dengue infection is typically achieved through serological tests (detection of dengue-specific antibodies) or molecular techniques (RT-PCR for viral RNA) [6]. However, these tests may not be readily available or affordable in many regions of India, particularly in rural and resource-limited settings. This limitation underscores the need for accessible and reliable diagnostic markers that can aid in the early detection of dengue fever.^[6]

Leukopenia, a condition characterized by a decreased white blood cell (WBC) count, has been observed in patients with dengue fever and is considered one of the hematological changes associated with the infection.^[7] The pathophysiology of leukopenia in dengue is thought to involve bone marrow suppression, peripheral destruction of leukocytes, and the effect of cytokines released during the immune response to the virus. As a potential early indicator of dengue infection, leukopenia could serve as a valuable clinical marker for diagnosis and management, especially in resource-constrained environments.^[8]

Previous studies have highlighted the occurrence of leukopenia in dengue fever, but its utility as a diagnostic marker remains underexplored, particularly in the Indian context.^[9,10]

Understanding the correlation between leukopenia and dengue infection could enhance clinical decision-making and patient outcomes by facilitating prompt diagnosis and appropriate care. So, the present study was conducted with an aim to evaluate the role of leukopenia as a diagnostic marker in dengue fever.

MATERIAL AND METHODS

Study Design and Setting

A prospective observational study was conducted at a tertiary care center in North India, in June 2024 under the department of General Medicine. The study aimed to explore the utility of leukopenia as a diagnostic marker in patients diagnosed with dengue fever.

Study Population

The study included 100 patients, aged 5 months to 65 years, who were suspected with dengue fever during the study period. Patients were recruited from the outpatient and inpatient departments of the hospital. Patients were excluded from the study if they had pre-existing hematological disorders or if they had other confirmed infections that could cause leukopenia, such as malaria or chikungunya. Additionally, patients who were on medications known to affect white blood cell counts were not included in the study.

Data Collection

After obtaining informed consent, detailed clinical history and demographic data were collected using a structured questionnaire. This included information on symptoms, duration of illness, and any prior medical conditions.

Laboratory Investigations

Blood samples were collected from all participants at the time of enrollment. The diagnosis of dengue fever was made using the Dengue card test, a rapid immunochromatographic assay that detects the presence of dengue NS1 antigen and IgM/IgG antibodies in the blood, providing a quick and reliable method for confirming dengue infection.^[11] This test was employed to ensure accurate and timely diagnosis for all participants in the study. Automated hematology analyzers were used to measure white blood cell counts and differential counts, and Leukopenia was defined as a total white blood cell count of less than 4,000-4500 cells/mm³. The presence and severity of leukopenia were recorded for each patient. Thrombocytopenia, or low platelet count, was classified as mild if the platelet count was between 100,000 and 150,000 platelets/mm³, moderate if the count was between 50,000 and 99,999 platelets/mm³, and severe if the count was less than 50,000 platelets/mm³, for both adults and children.^[12]

Statistical Analysis

Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean \pm standard deviation, and categorical variables were expressed as frequencies and percentages. The association between leukopenia and independent variables was evaluated using chi-square tests for categorical variables and t-tests for continuous variables. Sensitivity and specificity of leukopenia in diagnosing dengue were calculated, and odds ratios for various factors were assessed using logistic regression. A p-value of <0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants or their guardians before enrollment. Confidentiality and privacy of patient data were maintained throughout the study.

RESULTS

In this study of 100 dengue patients, the average age was 29.5 years, with a standard deviation of 18.3 years and an age range of 2 to 87 years. The leukopenia group (n = 78) had a slightly higher mean age of 30.2 years compared to the non-leukopenia group (n = 22), which had a mean age of 27.2 years, though this difference was not statistically significant (p = 0.523). The gender distribution showed a slight male predominance, with 56% of the total participants being male. In the leukopenia group, 55.1% were male, while in the non-leukopenia group, 59.1% were male, with no significant difference between the groups (p = 0.726). All participants experienced fever, a universal symptom of dengue in this cohort. Other common symptoms included headache, reported by 82% of patients, with similar prevalence in both the leukopenia (82.1%) and non-leukopenia (81.8%) groups (p = 0.826). Myalgia was noted in 75% of patients, slightly more common in the leukopenia group (76.9%) compared to the non-leukopenia group (68.2%), but this difference was not statistically significant (p = 0.447). Rash was observed in 41% of patients, with 42.3% in the leukopenia group and 36.4% in the non-leukopenia group, also showing no significant difference (p = 0.709). The mean duration of fever was 5.5 days, with a standard deviation of 1.5 days. The leukopenia group had a slightly longer average fever duration of 5.7 days compared to 5.1 days in the non-leukopenia group, although this difference did not reach statistical significance (p = 0.155). [Table 1]

The study analyzed key hematological parameters among 100 dengue patients, differentiating between those with and without leukopenia. The mean white blood cell (WBC) count for the entire cohort was 3,224.4 cells/mm³, with a range from 760 to 8,900 cells/mm³. A significant difference was observed between the leukopenia group and the non-leukopenia group, with mean WBC counts of 2,539.9 ± 828.1 cells/mm³ and 5,650.9 ± 1,329.3 cells/mm³, respectively, indicating a highly significant reduction in WBCs in the leukopenia group (p < 0.0001). The mean platelet count was 115.9 × 10³/mm³, ranging from 9 to 430 × 10³/mm³, with nearly identical mean values for both the leukopenia group (115.9 ± 79.5 × 10³/mm³) and the non-leukopenia group (116.3 ± 56.4 × 10³/mm³), resulting in no significant difference (p = 0.979). Hemoglobin levels across the cohort averaged 12.6 g/dL with a range of 7 to 18 g/dL. Regarding thrombocytopenia severity, 22% of patients experienced mild thrombocytopenia, with 23.1% in the leukopenia group and 18.2% in the non-leukopenia group (p = 0.237). Moderate thrombocytopenia was present in 27% of patients, with 29.5% in the leukopenia group compared to 18.2% in the non-leukopenia group. Severe thrombocytopenia was observed in 21% of the cohort, occurring in 16.7% of the leukopenia group and notably higher at 36.4% in the non-leukopenia group. Thrombocytopenia was absent in 30% of patients, with similar distributions in both the leukopenia (30.7%) and non-leukopenia (27.2%) groups. [Table 2]

The outcomes of the 100 dengue patients were assessed with respect to hospital stay, recovery rate, and complications, comparing the leukopenia and non-leukopenia groups. The mean duration of hospital stay was 7.6 ± 2.2 days overall. Patients in the leukopenia group had a significantly longer average hospital stay of 8.7 ± 2.1 days compared to 6.3 ± 1.6 days in the non-leukopenia group (p = 0.025), indicating that leukopenia was associated with prolonged hospitalization. The overall recovery rate was 85%, with 79.5% in the leukopenia group and a significantly higher rate of 95.5% in the non-leukopenia group (p = 0.041). This suggests that patients without leukopenia had a better recovery outcome. Complications were more prevalent in the leukopenia group. Bleeding occurred in 16% of the total cohort, with a higher incidence in the leukopenia group (17.9%) compared to the non-leukopenia group (9.1%), showing a significant association (p = 0.011). Shock was reported in 11% of patients, with similar rates between the leukopenia (11.5%) and non-leukopenia groups (9.1%), resulting in no significant difference (p = 0.231). Organ failure was observed in 6% of patients, occurring only in the leukopenia group (7.7%), with no cases in the non-leukopenia group, reflecting a significant difference (p = 0.034). [Table 3]

The logistic regression analysis examined various factors to determine their association with the likelihood of having dengue fever. Leukopenia had an odds ratio (OR) of 3.51, suggesting that patients with leukopenia were 3.51 times more likely to have dengue; however, this was not statistically significant (95% CI: 0.81 - 6.85, p = 0.202). Age showed an OR of 1.02, indicating a minimal, non-significant increase in odds with each additional year (95% CI: 0.98 - 1.06, p = 0.251). Gender had an OR of 1.13, implying no significant difference in the likelihood of having dengue between males and females (95% CI: 0.62 - 2.05, p = 0.721). The platelet count was significantly associated with the likelihood of dengue, with an OR of 0.97, indicating that higher platelet counts were associated with a reduced likelihood of having dengue (95% CI: 0.95 - 0.99, p = 0.011). The presence of a rash was associated with an OR of 1.55, suggesting that patients with a rash were 1.55 times more likely to have dengue, although this was not statistically significant (95% CI: 0.83 - 2.83, p = 0.181). [Table 4]

The diagnostic performance of leukopenia in relation to the Dengue card test was assessed using sensitivity and specificity analysis. Sensitivity, which reflects the ability of leukopenia to correctly identify patients with dengue, was calculated to be 93.3%. This indicates that 93.3% of patients with dengue were correctly identified as having leukopenia. Specificity, which reflects the ability of leukopenia to correctly identify patients without dengue, was found to be 68.0%. This means that 68.0% of patients without dengue were accurately identified as not having leukopenia. These results underscore that while leukopenia is highly sensitive, its moderate specificity suggests that it should be used in conjunction with other diagnostic methods for optimal accuracy. [Table 5]

Table 1: Baseline characteristics for the study participants (N=100)

Variable	Total (n = 100)	Leukopenia Group (n = 78)	Non-Leukopenia Group (n = 22)	p-value
	Frequency (%) / Mean ± SD			
Age (years)	29.5 ± 18.3	30.2 ± 17.7	27.2 ± 19.8	0.523
Gender				
Male	56 (56.0)	43 (55.1)	13 (59.1)	0.726
Female	44 (44.0)	35 (44.9)	9 (40.9)	

Symptoms				
Fever	100 (100.0)	78 (100.0)	22 (100.0)	1.000
Headache	82 (82.0)	64 (82.1)	18 (81.8)	0.826
Myalgia	75 (75.0)	60 (76.9)	15 (68.2)	0.447
Rash	41 (41.0)	33 (42.3)	8 (36.4)	0.709
Duration of Fever (days)	5.5 ± 1.5	5.7 ± 1.6	5.1 ± 1.4	0.155

Table 2: Laboratory parameters comparison for the study participants (N=100)

Parameter	Total (n = 100)	Leukopenia Group (n = 78)	Non-Leukopenia Group (n = 22)	p-value
	Frequency (%) / Mean ± SD (Range)			
WBC Count (cells/mm ³)	3224.4 ± 1608.1	2539.9 ± 828.1	5650.9 ± 1329.3	<0.0001
Platelet Count (x10 ³ /mm ³)	115.9 ± 74.8	115.9 ± 79.5	116.3 ± 56.4	0.979
Thrombocytopenia Severity				
Mild	22 (22.0)	18 (23.1)	4 (18.2)	0.237
Moderate	27 (27.0)	23 (29.5)	4 (18.2)	
Severe	21 (21.0)	13 (16.7)	8 (36.4)	
No	30 (30.0)	24 (30.7)	6 (27.2)	

Table 3: Outcome parameters among the study participants (N=100)

Outcome	Total (n = 100)	Leukopenia Group (n = 78)	Non-Leukopenia Group (n = 22)	p-value
	Frequency (%) / Mean ± SD			
Hospital Stay (days)	7.6 ± 2.2	8.7 ± 2.1	6.3 ± 1.6	0.025
Recovery Rate	85 (85.0)	62 (79.5)	21 (95.5)	0.041
Complications				
Bleeding	16 (16.0)	14 (17.9)	2 (9.1)	0.011
Shock	11 (11.0)	9 (11.5)	2 (9.1)	0.231
Organ Failure	6 (6.0)	6 (7.7)	0 (0.0)	0.034

Table 4: Logistic regression analysis for various factors to determine their association dengue

Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Leukopenia	3.51	0.81 - 6.85	0.202
Age	1.02	0.98 - 1.06	0.251
Gender	1.13	0.62 - 2.05	0.721
Platelet Count	0.97	0.95 - 0.99	0.011
Presence of Rash	1.55	0.83 - 2.83	0.181

Table 5: Sensitivity and specificity of leukopenia in diagnosing dengue

Variable	Dengue Card Test Positive (n=75)	Dengue Card Test Negative (n=25)
Leukopenia Present (n=78)	70	8
Leukopenia Absent (n=22)	5	17

DISCUSSION

In this study, we explored the diagnostic value of leukopenia in dengue fever and compared its performance with the Dengue card test. Our findings elucidate the role of leukopenia in dengue diagnosis, its correlation with clinical and laboratory parameters, and its impact on patient outcomes.

Our analysis showed no significant differences in age, gender distribution, or common symptoms between the leukopenia and non-leukopenia groups. The mean age was similar across both groups (30.2 years vs. 27.2 years, $p=0.523$), and gender distribution was comparable (55.1% males vs. 59.1%, $p=0.726$). This finding aligns with previous studies, which have also reported no significant differences in age and gender distribution among dengue patients with or without leukopenia.^[13,14]

The prevalence of symptoms such as fever, headache, myalgia, and rash was consistent across groups, reflecting a typical dengue symptom profile that is not influenced by leukopenia.^[15]

Our study found a significant difference in white blood cell (WBC) counts between the leukopenia

and non-leukopenia groups (2539.9 ± 828.1 cells/mm³ vs. 5650.9 ± 1329.3 cells/mm³, $p<0.0001$). This finding corroborates with other research, which highlights leukopenia as a common hematological abnormality in dengue fever, associated with a reduction in WBC counts.^[16] Conversely, platelet counts were similar between the groups (115.9 ± 79.5 x10³/mm³ vs. 116.3 ± 56.4 x10³/mm³, $p=0.979$), suggesting that while thrombocytopenia is a common feature in dengue, its presence does not significantly differentiate between leukopenia and non-leukopenia groups.^[17] The severity of thrombocytopenia was not significantly different between the groups, although a higher proportion of severe cases were observed in the non-leukopenia group, aligning with findings from other studies that indicate variable presentation of thrombocytopenia in dengue cases.^[18]

The leukopenia group had a significantly longer hospital stay (8.7 ± 2.1 days vs. 6.3 ± 1.6 days, $p=0.025$) and a lower recovery rate (79.5% vs. 95.5%, $p=0.041$), with increased complications such as bleeding and organ failure (17.9% vs. 9.1%, $p=0.011$; 7.7% vs. 0.0%, $p=0.034$). These results are

consistent with findings from other studies which suggest that leukopenia in dengue patients is associated with more severe disease outcomes and increased complications.^[19,20] The prolonged hospital stay and higher complication rates may be due to the increased severity of dengue cases in patients with leukopenia, reflecting the association between leukopenia and severe dengue manifestations.

Our odds ratio analysis revealed that leukopenia had an odds ratio of 3.51 (95% CI: 0.81 - 6.85, $p=0.202$), indicating a moderate association with dengue fever, though not statistically significant. This is consistent with some studies that have found varying degrees of association between leukopenia and dengue, suggesting that while leukopenia is a relevant marker, its diagnostic utility may be influenced by other factors.^[21] Platelet count, however, was a significant predictor with an odds ratio of 0.97 (95% CI: 0.95 - 0.99, $p=0.011$), underscoring its relevance in dengue diagnosis as previously documented.^[22]

The sensitivity of leukopenia for detecting dengue was calculated at 93.3%, indicating a high ability to correctly identify dengue cases. However, the specificity was 68.0%, suggesting that leukopenia may also be observed in some non-dengue cases. This moderate specificity aligns with previous research that has reported similar findings, where leukopenia, while highly sensitive, is not highly specific and should be used alongside other diagnostic methods.^[23,24] The high sensitivity demonstrates that leukopenia is a valuable marker for identifying dengue, but its moderate specificity indicates that it should not be relied upon solely for diagnosis.

CONCLUSION

Our study underscores the importance of leukopenia as a highly sensitive marker for dengue fever, although its moderate specificity suggests the need for a multi-faceted diagnostic approach. The association between leukopenia and more severe disease outcomes highlights its potential role in identifying severe cases of dengue. However, due to its moderate specificity, leukopenia should be complemented with other diagnostic tests to enhance diagnostic accuracy and patient management. These findings contribute to a more nuanced understanding of leukopenia's role in dengue fever and emphasize the need for integrated diagnostic strategies in clinical practice.

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