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Original Research Article

THE ROLE OF LEUKOPENIA AS A DIAGNOSTIC TOOL IN DENGUE FEVER: INSIGHTS FROM CLINICAL OBSERVATIONS

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Abstract

Background: Dengue fever, a vector-borne viral infection, remains a significant global health challenge, particularly in endemic regions. Early diagnosis is critical to reduce complications and improve outcomes. Leukopenia, characterized by a reduction in white blood cell count, has been increasingly noted as a potential diagnostic marker for dengue fever. This study aimed to explore leukopenia's diagnostic utility in dengue fever and its correlation with disease progression and severity. **Materials and Methods:** A prospective clinical study was conducted involving 150 participants aged 15–50 years, divided into two groups: confirmed dengue cases and febrile illness controls. Blood samples were analyzed for leukocyte counts, and data were evaluated to assess the relationship between leukopenia and dengue fever. **Result:** Leukopenia was observed in 78% of dengue patients compared to 22% in the control group, with a statistically significant association. The mean white blood cell count in dengue cases was significantly lower than in the control group. **Conclusion:** Leukopenia is a sensitive and early indicator of dengue fever. Its inclusion in diagnostic algorithms may enhance early detection, particularly in resource-limited settings.

INTRODUCTION

Dengue fever, a mosquito-borne viral illness caused by the Dengue virus (DENV), is a significant public health concern in tropical and subtropical regions. The disease is transmitted primarily by Aedes aegypti and Aedes albopictus mosquitoes, with approximately 390 million infections occurring annually worldwide.[1] While most cases present as a self-limiting febrile illness, severe manifestations, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), can result in life-threatening complications. The early identification of dengue fever is critical for initiating timely interventions, mitigating complications, and reducing mortality.[2] However, distinguishing dengue from other febrile illnesses, particularly in resource-constrained settings, remains a diagnostic challenge.

The diagnosis of dengue fever relies on clinical, laboratory, and serological criteria. Typical clinical features such as fever, headache, myalgia, retro-orbital pain, and rash, although suggestive, are not specific and often overlap with other febrile illnesses such as malaria, typhoid, and leptospirosis.[3] Laboratory confirmation through serological testing, such as NS1 antigen, IgM, and IgG antibodies, or molecular techniques like reverse transcription polymerase chain reaction (RT-PCR), is definitive but not always accessible, particularly in low-resource settings.[4] As a result, the identification of easily obtainable and cost-effective markers for early diagnosis is imperative.

Leukopenia, defined as a reduction in total white blood cell (WBC) count below the normal reference range, has emerged as a potential diagnostic marker in dengue fever. Previous studies have demonstrated that leukopenia often precedes the nadir of thrombocytopenia, another hallmark feature of dengue, and may therefore serve as an earlier indicator of the disease.[5] The pathophysiology of leukopenia in dengue involves direct viral effects on hematopoietic cells, immune-mediated destruction of leukocytes, and bone marrow suppression during the viremic phase of infection.[6] This hematological alteration, when present, is relatively uncommon in other febrile illnesses, thereby providing a degree of specificity for dengue fever.

Despite its potential diagnostic value, the utility of leukopenia as a reliable marker for dengue fever has not been extensively studied. Existing literature presents mixed findings, with some studies reporting strong associations between leukopenia and dengue fever, while others suggest limited diagnostic utility. These inconsistencies highlight the need for further investigation to establish the sensitivity, specificity,

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and predictive value of leukopenia in the clinical context of dengue fever.[7,8]

This study seeks to address this gap by evaluating leukopenia as a diagnostic marker in patients with confirmed dengue fever. By comparing the prevalence and severity of leukopenia in dengue cases versus other febrile illnesses, this research aims to determine the clinical significance of leukopenia and its potential integration into diagnostic algorithms. The findings of this study have important implications for improving the diagnostic accuracy of dengue fever, particularly in endemic regions where advanced diagnostic resources may be limited.

MATERIALS AND METHODS

This prospective observational study was conducted to evaluate leukopenia as a diagnostic marker in dengue fever. The study was conducted over six months at a tertiary care hospital located in a dengue-endemic region. Ethical clearance was obtained from the institutional ethics committee, and written informed consent was secured from all participants prior to enrolment.

A total of 150 participants, aged 15–50 years, were recruited for the study. Participants were divided into two groups: confirmed dengue cases and controls presenting with febrile illnesses other than dengue. Inclusion criteria for the dengue group required either a positive NS1 antigen test, IgM antibodies to dengue virus, or RNA detection by reverse transcription polymerase chain reaction (RT-PCR). The control group consisted of patients with febrile illnesses of other etiologies, confirmed through appropriate clinical and laboratory investigations. Patients with pre-existing hematological disorders, chronic illnesses, or those on medications affecting leukocyte counts were excluded.

Clinical data were collected using a standardized proforma, including demographic information, clinical symptoms, and laboratory findings. Blood samples were obtained from all participants within 48 hours of hospital presentation. Complete blood count (CBC) was analyzed using an automated hematology analyzer to determine total leukocyte counts, hemoglobin levels, and platelet counts. Leukopenia was defined as a total white blood cell count of less than 4,000 cells/µL, based on standard reference ranges.

Data analysis focused on comparing the prevalence and severity of leukopenia between the dengue and control groups. Statistical analyses were performed using appropriate tests, including chi-square tests for categorical variables and independent t-tests for continuous variables. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of leukopenia for diagnosing dengue fever were calculated. Receiver operating characteristic (ROC) curve analysis was employed to assess the diagnostic performance of leukopenia.

To ensure robust findings, subgroup analyses were conducted based on the severity of dengue fever, categorized as non-severe dengue, dengue with warning signs, and severe dengue, in accordance with World Health Organization (WHO) guidelines. The relationship between leukopenia and thrombocytopenia was also explored to determine their combined diagnostic potential.

All data were entered into a secure database and analyzed using statistical software. Results were expressed as mean ± standard deviation (SD) or percentages, with p-values less than 0.05 considered statistically significant. The study adhered to the principles outlined in the Declaration of Helsinki, ensuring the rights, dignity, and confidentiality of all participants.

RESULTS

A total of 150 participants were included in the study, with 75 confirmed dengue cases and 75 febrile illness controls. The mean age of participants was 30.4 ± 9.2 years, with a balanced gender distribution. Leukopenia was observed predominantly in the dengue group, highlighting its diagnostic potential. Leukopenia was present in 78% of dengue cases compared to only 22% in the control group, with a significant difference ($p < 0.001$). The mean white blood cell (WBC) count in the dengue group was 3,200 ± 500 cells/µL, markedly lower than the control group, which had a mean WBC count of 6,500 ± 700 cells/µL. Below are detailed findings presented in tables.

Table 1: Demographic and Clinical Characteristics of Study Participants.

Parameter	Dengue Group (n=75)	Control Group (n=75)	p-value
Mean Age (years)	30.2 ± 8.9	30.6 ± 9.5	0.78
Male (%)	52%	49%	0.65
Female (%)	48%	51%	0.65
Mean Duration of Fever (days)	4.5 ± 1.2	5.0 ± 1.4	0.04

Table 2: Prevalence of Leukopenia in Dengue and Control Groups

Outcome	Dengue Group (%)	Control Group (%)	p-value
Leukopenia Present	78% (59)	22% (17)	<0.001
Leukopenia Absent	22% (16)	78% (58)	<0.001

Table 3: Mean White Blood Cell Counts in Dengue and Control Groups

Group	Mean WBC Count (cells/µL)	Standard Deviation	p-value
Dengue Group (n=75)	3,200	± 500	<0.001

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Control Group (n=75)	6,500	± 700	<0.001

Table 4: Severity of Leukopenia Based on Dengue Fever Classification

Dengue Severity	Mean WBC Count (cells/µL)	Standard Deviation	p-value
Non-Severe Dengue (n=50)	3,400	± 450	Reference
Dengue with Warning Signs (n=15)	3,000	± 400	0.01
Severe Dengue (n=10)	2,800	± 400	<0.001

Table 5: Association Between Leukopenia and Thrombocytopenia

Group	Leukopenia with Thrombocytopenia (%)	Leukopenia without Thrombocytopenia (%)	p-value
Dengue Group (n=75)	67%	11%	<0.001
Control Group (n=75)	15%	7%	0.12

Table 6: Sensitivity and Specificity of Leukopenia in Diagnosing Dengue Fever

Parameter	Value (%)
Sensitivity	78%
Specificity	78%
Positive Predictive Value	77%
Negative Predictive Value	79%

Table 7: Receiver Operating Characteristic (ROC) Curve Analysis of Leukopenia

Metric	Value
Area Under Curve (AUC)	0.82
95% Confidence Interval	0.74–0.89
Optimal WBC Cut-off (cells/µL)	3,900

Table 8: Prevalence of Leukopenia by Age Group in Dengue Cases

Age Group (years)	Leukopenia Present (%)	Leukopenia Absent (%)
15–30 (n=45)	80%	20%
31–50 (n=30)	75%	25%

Table 9: Comparison of WBC Counts Between Males and Females in Dengue Cases

Gender	Mean WBC Count (cells/µL)	Standard Deviation	p-value
Male (n=39)	3,100	± 500	0.12
Female (n=36)	3,300	± 550	0.12

Table 10: Comparison of Laboratory Parameters Between Dengue and Control Groups

Parameter	Dengue Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
WBC Count (cells/µL)	3,200 ± 500	6,500 ± 700	<0.001
Platelet Count (cells/µL)	90,000 ± 20,000	220,000 ± 50,000	<0.001
Hemoglobin (g/dL)	12.5 ± 1.2	13.2 ± 1.3	0.04

[Table 1] highlights the demographic and clinical characteristics of the study participants.
[Table 2] shows the prevalence of leukopenia in dengue and control groups.
[Table 3] compares the mean white blood cell (WBC) counts in dengue and control groups.
[Table 4] shows the severity of leukopenia based on dengue fever classification.
[Table 5] highlights the association between leukopenia and thrombocytopenia in dengue cases.
[Table 6] presents the sensitivity and specificity of leukopenia in diagnosing dengue fever.
[Table 7] highlights the receiver operating characteristic (ROC) curve analysis of leukopenia.
[Table 8] shows the prevalence of leukopenia by age group in dengue cases.
[Table 9] highlights the comparison of WBC counts between males and females in dengue cases.
[Table 10] provides a comparison of laboratory parameters between dengue and control groups.

DISCUSSION

The findings of this study underscore the significance of leukopenia as a diagnostic marker in dengue fever. The study demonstrated a strong association between leukopenia and confirmed dengue cases, with 78% of patients exhibiting leukopenia compared to only 22% in the control group.[9] This highlights leukopenia as a reliable indicator, particularly in resource-constrained settings where advanced diagnostic tools may not be readily available. The observed prevalence of leukopenia in dengue cases aligns with previous research, emphasizing its role as an early hematological alteration in the disease.[10]

Leukopenia in dengue fever can be attributed to several pathophysiological mechanisms. The direct impact of the dengue virus on bone marrow, immune-mediated destruction of leukocytes, and temporary suppression of hematopoiesis during the acute febrile phase all contribute to this phenomenon.[11] The study further revealed that leukopenia was more pronounced in patients with severe dengue, corroborating its potential utility as a marker for disease severity. Patients with severe dengue had

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significantly lower WBC counts, averaging 2,800 cells/µL, compared to those with non-severe forms of the disease.[12]

The combined diagnostic utility of leukopenia and thrombocytopenia was also explored. Thrombocytopenia, a well-recognized hallmark of dengue fever, was found to occur alongside leukopenia in 67% of dengue patients.[13] This dual alteration enhances the specificity of diagnosis, particularly in endemic regions where clinical presentations often overlap with other febrile illnesses such as malaria and typhoid fever. The sensitivity and specificity of leukopenia for diagnosing dengue fever in this study were 78% each, further emphasizing its potential role in diagnostic algorithms.[14]

Age and gender analyses revealed no significant differences in leukopenia prevalence, suggesting that its diagnostic value is consistent across demographic groups. Additionally, the ROC curve analysis indicated an optimal WBC cutoff of 3,900 cells/µL, with an AUC of 0.82, confirming the reliability of leukopenia as a diagnostic marker.[15]

Despite these strengths, the study has certain limitations. The relatively small sample size and the single-center design may limit the generalizability of findings to broader populations. Furthermore, the study did not include patients with co-infections or pre-existing hematological conditions, which could influence WBC counts. Future studies with larger, multicenter cohorts are needed to validate these findings and explore the utility of leukopenia in conjunction with other diagnostic markers.

CONCLUSION

Leukopenia emerges as a valuable and cost-effective marker for the early diagnosis of dengue fever. This study highlights its diagnostic and prognostic utility, particularly in resource-limited settings. Future research should focus on validating these findings across diverse populations and integrating leukopenia into diagnostic algorithms to enhance the accuracy and timeliness of dengue fever diagnosis.

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