Journal Interdisciplinary Health

Volume 2 Issue 2, May 2026
DOI: https://doi.org/10.61099/jih.v2i2.252

Original Article

OPEN ACCESS

Association Between Platelet Count and Liver Enzymes in Critical Phase Dengue Patients: A Cross-Sectional Study

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Received: 2026-02-02 ○ Revised: 2026-03-25 ○ Received: 2026-04-02 ○ Published: 2026-05-05

ABSTRACT

Introduction: Dengue infection remains a major cause of hospitalization in tropical regions, particularly during the critical phase when plasma leakage, thrombocytopenia, and organ involvement increase the risk of severe complications. Hepatic dysfunction, reflected by elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT), frequently accompanies hematologic deterioration. However, the phase-specific association between platelet count and liver enzyme elevation remains insufficiently characterized. This study aimed to determine the association between platelet count and AST and ALT levels among patients in the critical phase of dengue infection.

Research Methodology: An analytic observational study with a cross-sectional design was conducted at Dr. TC Hillers Regional General Hospital, East Nusa Tenggara, Indonesia, between January and December 2025. A total of 68 patients meeting the WHO criteria for critical-phase dengue were included through consecutive sampling. Platelet count, AST, and ALT levels were extracted from medical records. Data distribution was assessed using the Shapiro–Wilk test. Pearson or Spearman correlation analysis was applied as appropriate. Statistical significance was set at $\alpha = 0.05$.

Results: The mean platelet count was 72.4 ± 28.7 $\times 10^3/\mu L$. Mean AST and ALT levels were 148.6 ± 64.2 U/L and 96.3 ± 41.8 U/L, respectively. Elevated AST was observed in 95.6% of patients, and elevated ALT in 85.3%. A significant negative correlation was found between platelet count and AST ($r = -0.412$, $p = 0.001$) and between platelet count and ALT ($r = -0.356$, $p = 0.003$).

Conclusion: Platelet decline is significantly associated with hepatic enzyme elevation during the critical phase of dengue infection. Integrated monitoring of platelet counts and transaminases may enhance risk stratification and support early identification of severe systemic involvement in endemic hospital settings.

Keywords: Alanine Transaminase; Aspartate Aminotransferases; Dengue; Liver Diseases; Thrombocytopenia

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INTRODUCTION

Dengue infection remains a major clinical and public health burden in tropical regions, particularly in Southeast Asia, where recurrent outbreaks place sustained pressure on hospital systems. In Indonesia, dengue continues to exhibit cyclical surges, resulting in significant morbidity and preventable mortality [1]. The most critical determinant of adverse outcome is progression to the critical phase, characterized by plasma leakage, thrombocytopenia, and potential shock. During this narrow therapeutic window, timely risk stratification is essential [2]. However, clinical assessment alone is insufficient to predict deterioration. Laboratory parameters, therefore, play a pivotal role in identifying patients at risk of severe complications. Among these, platelet count is routinely monitored as a hallmark indicator of disease progression [3]. At the same time, hepatic transaminases aspartate aminotransferase (AST) and alanine aminotransferase (ALT) reflect hepatic involvement, which has increasingly been recognized as a contributor to disease severity [4].

Accumulating evidence demonstrates that hepatic dysfunction is common in dengue infection. Several studies report that AST elevation occurs in nearly all hospitalized dengue patients, with ALT elevated in the majority of cases [5]. Notably, AST levels often exceed ALT levels, suggesting not only hepatocellular injury but also extrahepatic tissue involvement. Elevated transaminases have been associated with prolonged hospitalization, increased risk of bleeding, and progression to dengue shock syndrome [6]. In parallel, thrombocytopenia remains a defining laboratory abnormality in dengue, resulting from bone marrow suppression, immune-mediated destruction, and peripheral consumption. Previous investigations have reported negative correlations between platelet count and AST levels, implying that worsening thrombocytopenia may coincide with greater hepatic injury. However, the strength and consistency of this association vary across studies [7].

Despite these findings, the relationship between platelet count and liver enzyme elevation remains incompletely characterized, particularly during the critical phase of dengue [8]. Many published studies combine febrile, critical, and recovery phases into a single analytic framework, potentially diluting phase-specific pathophysiological dynamics [9]. Furthermore, several studies emphasize hematocrit or overall severity classification rather than directly examining the quantitative association between thrombocytopenia and transaminase levels [10]. Evidence from Indonesian regional hospitals, especially in eastern provinces with high endemicity, remains limited. This lack of phase- and context-specific analysis limits the development of laboratory-based risk-stratification models tailored to critical-phase management [11].

The explicit research gap, therefore, lies in the absence of focused analytic evaluation of the association between platelet count and AST and ALT levels exclusively during the critical phase of dengue infection. Without isolating this phase, it remains unclear whether declining platelet counts can serve as a surrogate marker for concurrent hepatic involvement at the moment when clinical deterioration is most likely to occur. Addressing this gap is clinically relevant because laboratory integration could enhance early warning systems and optimize monitoring protocols in resource-constrained hospital settings.

This study offers novelty in two principal aspects. First, it restricts analysis to confirmed critical-phase dengue patients, thereby minimizing phase-related confounding and capturing pathophysiological interactions at their peak intensity. Second, it simultaneously evaluates the relationship between platelet count and both AST and ALT using an analytic cross-sectional framework within a regional referral hospital in an endemic eastern Indonesian setting. By

contextualizing findings within a high-burden environment, this study contributes locally grounded evidence to the broader discourse on laboratory predictors of dengue severity. Accordingly, the objective of this study is to determine the association between platelet count and AST levels, and between platelet count and ALT levels, among patients with critical-phase dengue. Through systematic laboratory analysis, this research seeks to clarify whether thrombocytopenia correlates significantly with hepatic enzyme elevation and to assess its potential utility as an integrated marker of disease severity during the critical phase.

MATERIALS AND METHODS

Study Design

This study employed an analytic observational design using a cross-sectional approach. The cross-sectional framework was selected because the objective was to determine the association between platelet count and liver enzyme levels (AST and ALT) measured during the critical phase of dengue infection without implementing intervention or longitudinal follow-up. This design allows simultaneous assessment of exposure (platelet count) and outcomes (AST and ALT levels) within a defined time frame, minimizing temporal bias while providing an efficient evaluation of laboratory correlations in hospitalized patients.

Setting and Participants

The study was conducted at Dr. TC Hillers Regional General Hospital, Sikka Regency, East Nusa Tenggara Province, Indonesia. This hospital serves as a regional referral center in a dengue-endemic area. Data collection was performed between January and December 2025. Inclusion criteria were: (1) patients diagnosed with dengue infection based on clinical criteria and laboratory confirmation (NS1 antigen and/or IgM/IgG serology), (2) classified as being in the critical phase according to WHO criteria (day 3–7 of illness with evidence of plasma leakage and thrombocytopenia), and (3) having complete laboratory records including platelet count, AST, and ALT measured during the critical phase. Exclusion criteria were: (1) patients with pre-existing chronic liver disease, viral hepatitis, or known hepatotoxic drug exposure, (2) patients with hematological disorders affecting platelet count, and (3) incomplete medical records.

Sampling Technique

A consecutive sampling technique was applied, in which all eligible patients meeting the inclusion criteria during the study period were enrolled until the required sample size was achieved. Sample size was calculated using the formula for correlation studies:

$$n = [(Z\alpha + Z\beta)^2 / (0.5 \times \ln((1+r)/(1-r)))^2] + 3$$

Assuming a minimum expected correlation coefficient (r) of 0.35 based on prior studies, a confidence level of 95% ($Z\alpha = 1.96$), and a statistical power of 80% ($Z\beta = 0.84$), the minimum required sample size was 62 subjects. To compensate for potential incomplete data, an additional 10% was added, resulting in a final minimum sample size of 68 participants.

Variables and Measurement

Independent Variable: Platelet count, defined as the number of platelets per microliter (µL) of blood measured using an automated hematology analyzer during the critical phase. Thrombocytopenia was defined as a platelet count <150,000/µL. Dependent Variables: Serum AST and ALT levels (U/L) measured using an automated clinical chemistry analyzer during the same phase. Elevated AST and ALT were defined as values exceeding the upper reference limit established by the hospital laboratory.

Validity and Reliability

All laboratory measurements were performed using calibrated automated analyzers routinely subjected to internal and external quality control procedures. The hematology and biochemistry analyzers undergo daily calibration and periodic validation in accordance with manufacturer standards and hospital laboratory accreditation protocols, ensuring analytical validity and reliability.

Data Source

This study used secondary data extracted from hospital medical records and laboratory information systems. Data were collected by reviewing eligible patients' medical records using a structured data extraction form. Variables recorded included demographic characteristics, day of illness, platelet count, AST, and ALT values during the critical phase. To ensure data accuracy, double-entry verification was conducted. Discrepancies were resolved by cross-checking against the original laboratory reports. Quality control measures included standardized data extraction procedures, training of data collectors, double-checking of laboratory values, and exclusion of incomplete records. Data cleaning was performed before statistical analysis to identify outliers and inconsistencies.

Data Analysis

Data were analyzed using IBM SPSS Statistics version 26. Descriptive statistics were used to summarize patient characteristics and laboratory parameters. Continuous variables were presented as mean ± standard deviation (SD) for normally distributed data or as median (interquartile range) for non-normally distributed data. Categorical variables were expressed as frequencies and percentages. Normality of data distribution was assessed using the Shapiro–Wilk test. For bivariate analysis, Pearson's correlation was used for normally distributed variables. In contrast, Spearman's rank correlation was used to assess the association between platelet count and AST and ALT levels, given their non-normal distributions. The level of statistical significance was set at $\alpha = 0.05$ with a 95% confidence interval.

Ethical Approval

Ethical clearance for this study was obtained from the Health Research Ethics Committee of Dr. TC Hillers Regional General Hospital. The study protocol was approved under reference number: 123/KEPK-RSUD/2025. As this research used secondary medical record data, the ethics committee waived informed consent; however, patient confidentiality and data anonymity were strictly maintained throughout the study in accordance with ethical research standards.

RESULTS

Table 1. Baseline Characteristics of Critical Phase Dengue Patients (n = 68)

Variable	Category / Statistic	n (%) / Mean ± SD
Age (years)	Mean ± SD	21.8 ± 9.6
Sex	Male	38 (55.9%)
	Female	30 (44.1%)
Platelet count (×10³/μL)	Mean ± SD	72.4 ± 28.7
	<100 ×10³/μL	52 (76.5%)
AST (U/L)	Mean ± SD	148.6 ± 64.2
ALT (U/L)	Mean ± SD	96.3 ± 41.8
Elevated AST	> Upper normal limit	65 (95.6%)
Elevated ALT	> Upper normal limit	58 (85.3%)

E-ISSN: 3109-0281

A total of 68 patients with critical phase dengue were included in the analysis. The mean age was 21.8 ± 9.6 years, with a slight predominance of male patients (55.9%). The mean platelet count during the critical phase was 72.4 ± 28.7 ×10³/µL, and the majority of patients (76.5%) had platelet levels below 100 ×10³/µL, indicating marked thrombocytopenia. Liver enzyme levels were elevated in most patients. The mean AST level (148.6 ± 64.2 U/L) was higher than the mean ALT level (96.3 ± 41.8 U/L). Elevated AST was observed in 95.6% of patients, while elevated ALT occurred in 85.3%, suggesting frequent hepatic involvement during the critical phase of dengue infection.

Table 2. Analysis of the Association Between Platelet Count and Liver Enzymes

Variables	Correlation Coefficient (r)	p-value	Interpretation
Platelet Count vs AST	-0.412	0.001	Moderate negative correlation
Platelet Count vs ALT	-0.356	0.003	Weak-to-moderate negative correlation

Bivariate analysis demonstrated a statistically significant negative correlation between platelet count and AST levels (r = -0.412, p = 0.001). This finding indicates that lower platelet counts were associated with higher AST levels during the critical phase. Similarly, platelet count showed a statistically significant negative correlation with ALT levels (r = -0.356, p = 0.003). Although the correlation was slightly weaker than that with AST, the association remains clinically relevant. These results suggest that worsening thrombocytopenia coincides with increasing hepatic enzyme elevation, supporting the hypothesis that platelet decline may parallel hepatic involvement during the critical phase of dengue infection.

The findings demonstrate a consistent pattern of significant hepatic involvement during the critical phase of dengue infection, accompanied by marked thrombocytopenia. The majority of patients presented with substantially reduced platelet counts, reinforcing the established role of thrombocytopenia as a central hematological manifestation during the plasma leakage phase. Concurrently, elevated AST and ALT levels were observed in most cases, with AST showing higher mean values compared to ALT. This disproportionate elevation suggests not only hepatocellular injury but also possible extrahepatic tissue involvement, reflecting the systemic inflammatory response characteristic of severe dengue. The bivariate analysis further reveals a statistically significant negative correlation between platelet count and both AST and ALT levels. This inverse relationship indicates that as platelet counts decline, transaminase levels tend to increase. Clinically, this pattern suggests a parallel progression between hematologic deterioration and hepatic injury during the critical phase. The stronger correlation observed with AST may imply broader tissue damage beyond the liver, consistent with dengue-related myocyte and endothelial involvement. Collectively, these findings support integrating platelet count and liver enzyme monitoring as complementary laboratory indicators to assess disease severity during the critical phase of dengue infection.

DISCUSSION

This study demonstrates a statistically significant inverse association between platelet count and liver enzyme levels (AST and ALT) among patients in the critical phase of dengue infection. Marked thrombocytopenia was consistently observed alongside elevated transaminases, with AST showing a stronger correlation compared to ALT. These findings indicate that hematologic deterioration and hepatic involvement occur concurrently during the critical phase, suggesting an interconnected pathophysiological process rather than isolated organ dysfunction [12]. The data support the premise that declining platelet levels may parallel

the magnitude of systemic inflammatory injury, particularly hepatic stress, at the time when the risk of shock and plasma leakage is highest. Importantly, by restricting analysis to the critical phase, this study captures laboratory dynamics at the peak of disease severity [13]. This phase-specific approach strengthens the inference that thrombocytopenia is not merely a diagnostic marker of dengue but may reflect broader systemic injury, including hepatic involvement. The stronger association observed with AST further suggests that transaminase elevation during severe dengue may represent multisystem tissue injury beyond hepatocellular damage alone [14].

The observed inverse correlation between platelet counts and transaminase levels can be interpreted within the framework of dengue immunopathogenesis[15]. During the critical phase, antibody-dependent enhancement (ADE) and dysregulated immune activation amplify viral replication within monocytes and macrophages [16]. This cascade triggers excessive cytokine release, endothelial activation, and increased vascular permeability [17]. The resulting plasma leakage and systemic inflammation contribute to both peripheral platelet destruction and hepatic injury [18]. Thrombocytopenia in dengue arises through multiple mechanisms: bone marrow suppression, immune-mediated platelet destruction, peripheral consumption, and platelet aggregation secondary to endothelial damage [19]. Simultaneously, hepatic injury may result from direct viral invasion of hepatocytes, immune-mediated cytotoxicity, hypoxic injury due to plasma leakage, and systemic inflammatory stress. The stronger correlation between platelet counts and AST compared to ALT is theoretically coherent, as AST is present not only in hepatocytes but also in skeletal muscle, myocardium, and erythrocytes [20]. Thus, elevated AST may reflect diffuse tissue injury rather than isolated hepatic dysfunction [21].

Conceptually, these findings suggest that platelet decline during the critical phase may function as a surrogate marker of systemic inflammatory burden [22]. Rather than interpreting thrombocytopenia solely as a bleeding risk indicator, it may be viewed as a hematologic signal of multisystem involvement [23]. This integrated interpretation shifts the clinical perspective from organ-specific monitoring to a systems-based understanding of dengue severity [24]. From a systems biology standpoint, dengue severity reflects a networked inflammatory process in which vascular integrity, coagulation pathways, immune activation, and organ function are tightly interlinked [25]. The significant correlation identified in this study reinforces the concept that hematologic and hepatic parameters should not be assessed independently. Instead, their interaction may provide a more accurate representation of disease trajectory during the critical phase [26].

Strengths and Limitations

A major strength of this study lies in its phase-specific analytic focus. By limiting inclusion to patients in the critical phase, the study minimizes temporal heterogeneity that often confounds dengue research. Many prior studies combine febrile, critical, and recovery phases, potentially diluting associations due to shifting pathophysiological states. This targeted approach enhances internal validity and strengthens the conceptual linkage between thrombocytopenia and hepatic injury at the peak of disease severity. Another strength is the use of standardized laboratory measurements conducted in an accredited hospital setting, which ensures analytical reliability. The analytic cross-sectional design also enabled efficient evaluation of correlations in a real-world clinical environment in an endemic region, providing context-specific evidence from the eastern Indonesian area, which is underrepresented in dengue research. However, several limitations must be acknowledged. First, the cross-sectional design precludes causal inference. Although a significant association was identified, the temporal direction between platelet decline and transaminase elevation cannot be definitively established. Longitudinal studies would be required to determine whether thrombocytopenia precedes, parallels, or predicts progression of hepatic injury. Second, the reliance on secondary medical record data may introduce information bias, including variability in the timing of laboratory testing relative to symptom onset. Although the inclusion criteria required measurement during the critical phase, subtle intra-phase timing differences may influence enzyme levels. Third, potential confounders, such as viral serotype, nutritional status,

and inflammatory markers, were not incorporated into the multivariable analysis, limiting deeper mechanistic inference. Despite these limitations, the study provides a meaningful conceptual contribution by reinforcing a systems-based interpretation of dengue severity. The integration of platelet counts and transaminase levels as interrelated markers may inform risk stratification strategies, particularly in resource-limited settings where advanced biomarkers are unavailable. Systemically, incorporating combined laboratory monitoring protocols during the critical phase may enhance early detection of deterioration, optimize triage decisions, and improve allocation of intensive care resources. This study advances the conceptual understanding of dengue pathophysiology by demonstrating that thrombocytopenia and hepatic enzyme elevation are interdependent manifestations of systemic inflammatory injury during the critical phase. Future research employing longitudinal and multivariable designs is warranted to refine predictive models and validate integrated laboratory indices for clinical application.

CONCLUSIONS

This study confirms a statistically significant inverse association between platelet count and liver enzyme levels (AST and ALT) among patients in the critical phase of dengue infection. Lower platelet counts were consistently associated with higher transaminase levels, indicating that hematologic deterioration parallels hepatic involvement during the period of greatest clinical instability. The stronger correlation observed with AST suggests that transaminase elevation during critical dengue may reflect broader systemic tissue injury rather than isolated hepatocellular damage. These findings directly address the study objective by demonstrating that thrombocytopenia is significantly associated with hepatic enzyme elevation in patients with critical-phase dengue. Clinically, platelet count and transaminase levels should be interpreted as integrated laboratory indicators rather than isolated parameters.

From a policy and systems perspective, hospitals in dengue-endemic regions should incorporate combined monitoring of platelet count and liver enzymes into standardized critical-phase management protocols. Early identification of concurrent thrombocytopenia and transaminase elevation may improve risk stratification, guide closer hemodynamic surveillance, and optimize timely referral to higher-level care, thereby reducing preventable complications and mortality.

Ethical Considerations

This study was conducted in accordance with the principles of the Declaration of Helsinki and applicable national research ethics guidelines. Ethical approval was obtained from the Health Research Ethics Committee of Dr. TC Hillers Regional General Hospital, Sikka Regency (Approval No: 123/KEPK-RSUD/2025). As the study used secondary data extracted from medical records without direct patient contact, the ethics committee formally waived the requirement for written informed consent. All data were anonymized before analysis to ensure confidentiality. No personal identifiers were recorded, and access to the dataset was restricted to the research team.

Funding Statement

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The study was conducted independently as part of an academic research requirement.

Conflict of Interest

The authors declare that there are no conflicts of interest related to this study. The research was conducted without any financial or commercial relationships that could be construed as a potential conflict of interest.

Authors' Contributions

Maria M. Barek Telumaa: Conceptualization; Methodology; Data Curation; Formal Analysis; Investigation; Writing – Original Draft; Visualization.

Nur Ismia: Supervision; Methodology; Validation; Writing – Review & Editing; Project

Administration.
Andi Heriadi Pallogea: Supervision; Validation; Writing – Review & Editing; Resources.

Acknowledgments

The authors express their sincere gratitude to the management and laboratory staff of Dr. TC Hillers Regional General Hospital for facilitating access to clinical and laboratory data. Appreciation is also extended to the academic faculty of the Medical Laboratory Technology Program for their scholarly guidance and constructive feedback throughout the research process.

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