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Liver Function Abnormalities in Patients with Dengue Fever: A Hospital-Based Observational Study.

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Abstract

Background: Dengue is a major mosquito-borne viral infection with a broad clinical spectrum ranging from uncomplicated febrile illness to severe dengue characterized by plasma leakage, severe bleeding, shock, and multiorgan dysfunction. Hepatic involvement is a recognized complication ranging from mild transaminase elevation to acute liver failure. Aspartate aminotransferase (AST) is frequently elevated more prominently than alanine aminotransferase (ALT). ***Methods:*** A hospital-based observational study was conducted among 100 laboratory-confirmed dengue fever patients admitted to a tertiary care hospital. Demographic data, clinical presentation, hematological parameters, and liver function tests (AST, ALT, total/direct bilirubin, alkaline phosphatase, serum albumin, INR) were analyzed across severity categories. ***Results:*** Of the 100 patients (mean age 31.8 ± 12.4 years; 62% male), hepatic biochemical abnormalities were present in 82%. AST elevation was the most frequent hepatic abnormality (76%), followed by ALT elevation (61%). Moderate-to-marked AST elevation (>3× ULN) occurred in 31% of patients. Patients with severe dengue (18%) had significantly higher median AST (318 vs 86 U/L, $p < 0.001$) and ALT (226 vs 69 U/L, $p < 0.001$) compared to non-severe cases. Hyperbilirubinemia, hypoalbuminemia, and prolonged INR were significantly more common in severe dengue. ***Conclusion:*** Hepatic biochemical abnormalities are highly prevalent in dengue fever, with AST elevation serving as a sensitive early indicator of liver involvement. Systematic monitoring of liver function parameters is essential for identifying high-risk patients and predicting clinical severity.

Keywords: dengue fever; dengue virus; hepatic dysfunction; AST; ALT; liver function tests; thrombocytopenia; severe dengue; acute liver injury.

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INTRODUCTION

Dengue is a viral infection caused by the dengue virus (DENV, serotypes 1–4) and transmitted predominantly by Aedes mosquitoes, representing a major public health problem in tropical and subtropical regions. The clinical spectrum ranges from an uncomplicated self-limiting febrile illness to severe dengue characterized by plasma leakage, severe bleeding, fluid accumulation, shock, and severe organ impairment [1].

Although thrombocytopenia and plasma leakage are widely recognized hallmark features of dengue infection, hepatic involvement is an increasingly appreciated component of disease pathogenesis. Liver injury during dengue virus infection occurs through several synergistic mechanisms, including direct viral cytotoxicity on hepatocytes and Kupffer cells, immune-mediated inflammatory injury, hypoxic/ischemic damage secondary to circulatory collapse or shock, and systemic inflammatory response syndrome [1, 2].

The most frequently observed biochemical abnormality is an elevation of serum aminotransferases. Crucially, aspartate aminotransferase (AST) increases earlier and more prominently than alanine aminotransferase (ALT) in dengue fever, a pattern distinct from classical viral hepatitis [2]. Other associated biochemical alterations include hyperbilirubinemia, hypoalbuminemia, elevated alkaline phosphatase (ALP), and prolonged prothrombin time / international normalized ratio (INR). In severe cases, acute hepatic injury can progress to fulminant acute liver failure [3].

Systematic meta-analyses report AST abnormalities in approximately 75% of patients with dengue fever and up to 80% in severe dengue, while ALT abnormalities occur in 52% to 54% of cases [2]. Regional Indian studies similarly demonstrate substantial hepatic involvement, with transaminase elevations exceeding 90% and strong correlations with disease severity [4].

Given that hepatic patterns vary by serotype, host immunity, comorbidities, and population dynamics, this study evaluated the pattern, frequency, and severity of liver function test (LFT) abnormalities in hospitalized dengue patients and examined their correlation with clinical severity and outcomes.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based observational study was conducted in the Department of General Medicine at Siddhartha Medical College / Government General Hospital, Vijayawada, Andhra Pradesh, India, over a 12-month period from 2021 to 2022.

Study Population and Eligibility

Patients aged ≥18 years admitted with laboratory-confirmed dengue fever (positive dengue NS1 antigen and/or IgM antibody testing by ELISA) who provided written informed consent were consecutively enrolled.

Exclusion criteria were: (a) pre-existing chronic liver disease or cirrhosis; (b) acute viral hepatitis A, B, C, or E co-infections; (c) alcoholic liver disease; (d) hepatic malignancy; (e) exposure to known hepatotoxic medications prior to admission; (f) underlying systemic conditions independently causing acute hepatitis; and (g) incomplete laboratory parameters.

Data Collection and Laboratory Protocols

A standardized proforma was utilized to document demographic data, fever duration, clinical symptoms (headache, myalgia, retro-orbital pain, abdominal pain, nausea/vomiting, bleeding manifestations, hepatomegaly), and vital signs. Laboratory testing at admission included complete blood counts, serial platelet monitoring, hematocrit, AST, ALT, total and direct bilirubin, ALP, total protein, serum albumin, and prothrombin time / INR using automated analyzer systems.

Definition of Hepatic Dysfunction

Hepatic dysfunction was defined as any serum liver function test parameter exceeding the institutional laboratory upper limit of normal (ULN; AST >40 U/L, ALT >40 U/L, Total Bilirubin >1.2 mg/dL, Direct Bilirubin >0.3 mg/dL, ALP >120 U/L, Albumin <3.5 g/dL, INR >1.2). Severity of transaminase elevation was categorized as follows:

- Normal: ≤1× ULN (≤40 U/L)
- Mild elevation: >1× to 3× ULN (41–120 U/L)
- Moderate elevation: >3× to 10× ULN (121–400 U/L)
- Severe elevation: >10× ULN (>400 U/L)

Assessment of Dengue Severity

Disease severity was classified into non-severe dengue (with or without warning signs) and severe dengue according to the World Health Organization (WHO) clinical criteria [6, 7]. Severe dengue was defined by plasma leakage leading to shock or fluid accumulation with respiratory distress, severe bleeding, or severe organ impairment (including AST/ALT >1000 U/L, impaired consciousness, or cardiac failure).

Statistical Analysis

Data were compiled and analyzed using IBM SPSS Statistics for Windows (Version 26.0). Continuous variables were tested for normality using the Kolmogorov-Smirnov test and expressed as mean ± standard deviation (SD) for normally distributed data or median with interquartile range (IQR) for non-parametric data. Categorical variables were summarized as absolute counts and percentages.

Comparative analyses between non-severe and severe dengue groups utilized Student's t-test or Mann-Whitney U test for continuous variables, and Chi-square test or Fisher's exact test for categorical variables. Multivariable logistic regression was performed to evaluate independent association between severe transaminase elevation and severe dengue outcomes. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

A total of 100 hospitalized patients with laboratory-confirmed dengue fever were evaluated. The mean age of the cohort was 31.8 ± 12.4 years (range: 18–68 years) with a male predominance (62.0% male vs 38.0% female).

The mean duration of fever prior to presentation was 4.8 ± 1.7 days. The baseline clinical and demographic characteristics are summarized in Table 1.

Table 1. Baseline demographic and clinical characteristics of study participants (n = 100)

Characteristic	Value (n = 100)
Age, mean ± SD (years)	31.8 ± 12.4
Age range (years)	18–68
Male, n (%)	62 (62.0%)
Female, n (%)	38 (38.0%)
Fever duration, mean ± SD (days)	4.8 ± 1.7
Headache, n (%)	72 (72.0%)
Myalgia, n (%)	68 (68.0%)
Nausea / Vomiting, n (%)	46 (46.0%)
Abdominal pain, n (%)	28 (28.0%)
Bleeding manifestations, n (%)	17 (17.0%)
Hepatomegaly, n (%)	12 (12.0%)
Severe dengue, n (%)	18 (18.0%)
Diabetes mellitus, n (%)	9 (9.0%)
Hypertension, n (%)	11 (11.0%)

Overall, 82.0% of patients demonstrated at least one abnormal liver function parameter. AST elevation was the most prevalent abnormality (76.0%), occurring significantly more frequently than ALT elevation (61.0%). Moderate-to-severe AST elevation (>3× ULN) was detected in 31.0% of patients, whereas ALT >3× ULN occurred in 19.0% (Table 2).

Table 2. Frequency and pattern of liver function abnormalities (n = 100)

Liver Function Parameter	Cut-off / Threshold	n (%)
AST elevation	>40 U/L	76 (76.0%)
ALT elevation	>40 U/L	61 (61.0%)
AST >3 × ULN	>120 U/L	31 (31.0%)
ALT >3 × ULN	>120 U/L	19 (19.0%)
Total bilirubin elevation	>1.2 mg/dL	14 (14.0%)
Direct bilirubin elevation	>0.3 mg/dL	18 (18.0%)
Alkaline phosphatase (ALP) elevation	>120 U/L	16 (16.0%)
Hypoalbuminemia	<3.5 g/dL	22 (22.0%)
Prolonged INR	>1.2	15 (15.0%)
Any LFT abnormality	≥1 abnormal parameter	82 (82.0%)

Comparison of hepatic parameters according to WHO disease severity revealed striking differences (Table 3). Median AST levels were nearly fourfold higher in severe dengue compared with non-severe dengue (318 [IQR 176–624] U/L vs 86 [IQR 58–142] U/L, $p < 0.001$). Similarly, median ALT levels were markedly elevated in severe disease (226 [IQR 128–418] U/L vs 69 [IQR 45–112] U/L, $p < 0.001$). Patients with severe dengue also demonstrated significantly higher rate of hyperbilirubinemia, elevated ALP, hypoalbuminemia (mean 3.21 ± 0.51 vs 3.72 ± 0.42 g/dL, $p < 0.001$), and INR prolongation.

Table 3. Comparison of liver function parameters according to dengue severity

Parameter	Non-severe Dengue (n = 82)	Severe Dengue (n = 18)	p-value
AST, median (IQR), U/L	86 (58–142)	318 (176–624)	<0.001
ALT, median (IQR), U/L	69 (45–112)	226 (128–418)	<0.001
Total bilirubin, median (IQR), mg/dL	0.8 (0.6–1.0)	1.3 (0.9–2.0)	0.002
Direct bilirubin, median (IQR), mg/dL	0.25 (0.18–0.36)	0.48 (0.30–0.82)	0.004
ALP, median (IQR), U/L	94 (78–116)	128 (102–161)	0.006
Albumin, mean ± SD, g/dL	3.72 ± 0.42	3.21 ± 0.51	<0.001
INR, median (IQR)	1.06 (1.01–1.11)	1.24 (1.13–1.38)	<0.001
AST >3 × ULN, n (%)	18 (22.0%)	13 (72.2%)	<0.001
ALT >3 × ULN, n (%)	10 (12.2%)	9 (50.0%)	<0.001

When stratifying patients by transaminase status, elevated aminotransferases were associated with significantly lower platelet counts (67 ± 29 vs 108 ± 32 × 10^9/L, $p < 0.001$), higher hematocrit (42.7 ± 5.1 vs 39.8 ± 4.2%, $p = 0.009$), longer fever duration (5.0 ± 1.7 vs 4.1 ± 1.4 days, $p = 0.015$), higher rates of bleeding (21.1% vs 4.2%, $p = 0.049$), and severe dengue classification (22.4% vs 4.2%, $p = 0.047$) (Table 4).

Table 4. Association between aminotransferase elevation and clinical/hematological parameters

Variable	Normal AST/ALT (n = 24)	Elevated AST/ALT (n = 76)	p-value
Platelet count, ×10⁹/L, mean ± SD	108 ± 32	67 ± 29	<0.001
Hematocrit, %, mean ± SD	39.8 ± 4.2	42.7 ± 5.1	0.009
Fever duration, days, mean ± SD	4.1 ± 1.4	5.0 ± 1.7	0.015
Severe dengue, n (%)	1 (4.2%)	17 (22.4%)	0.047
Bleeding manifestations, n (%)	1 (4.2%)	16 (21.1%)	0.049
Abdominal pain, n (%)	3 (12.5%)	25 (32.9%)	0.048
Hypotension / Shock, n (%)	0 (0.0%)	9 (11.8%)	0.079
ICU admission, n (%)	0 (0.0%)	8 (10.5%)	0.106

Evaluation of outcomes across categories of enzyme elevation demonstrated a step-wise increase in severe dengue (from 4.2% in normal LFTs to 44.4% in AST/ALT >10× ULN), ICU admission (from 0.0% to 33.3%), and mortality (0.0% to 11.1%; overall $p < 0.001$) (Table 5). Overall mortality was 2.0% (n = 2), both occurring in patients with severe transaminase elevation and acute liver injury.

Table 5. Distribution according to severity of liver enzyme elevation and clinical outcome

Degree of Enzyme Elevation	Total, n (%)	Severe Dengue, n (%)	ICU Admission, n (%)	Mortality, n (%)
Normal (≤1 × ULN)	24 (24.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)
Mild elevation (>1 to 3 × ULN)	45 (45.0%)	5 (11.1%)	1 (2.2%)	0 (0.0%)
Moderate elevation (>3 to 10 × ULN)	22 (22.0%)	8 (36.4%)	4 (18.2%)	1 (4.5%)
Severe elevation (>10 × ULN)	9 (9.0%)	4 (44.4%)	3 (33.3%)	1 (11.1%)
Total Cohort	**100 (100.0%)**	**18 (18.0%)**	**8 (8.0%)**	**2 (2.0%)**

DISCUSSION

The present study demonstrates that hepatic biochemical abnormalities are exceptionally common among hospitalized dengue patients, affecting 82.0% of the cohort. The predominant manifestation is aminotransferase elevation, with AST exhibiting a higher frequency (76.0% vs 61.0%) and greater magnitude of elevation than ALT. These findings align with global literature and clinical WHO guidance recognizing liver involvement as a primary extrahematological feature of dengue infection [1, 6].

The striking preferential elevation of AST over ALT in dengue contrasts sharply with classic acute viral hepatitis A, B, or E, where ALT typically predominates due to higher hepatocyte specificity. In dengue, AST is also released from extrahepatic tissue sources, including damaged myocytes and lymphoreticular cells affected by viral tropism and systemic inflammation [2, 5]. Furthermore, mitochondrial injury in hepatocytes induced by dengue virus non-structural protein 1 (NS1) preferentially releases mitochondrial AST [1, 3].

Our findings confirm a potent positive correlation between the severity of hepatic dysfunction and overall dengue clinical severity. Patients with severe dengue exhibited markedly higher transaminases, bilirubin, ALP, and INR, alongside significant hypoalbuminemia. Hypoalbuminemia in severe dengue reflects both compromised hepatic synthetic capacity and increased capillary permeability driven by endothelial activation and plasma leakage [1, 4].

Biochemical monitoring provides crucial prognostic value. In our cohort, AST or ALT >10× ULN was associated with a 44.4% rate of severe dengue, a 33.3% ICU admission rate, and an 11.1% mortality rate. Similar observational studies from Asia and Latin America underscore that serial AST/ALT monitoring serves as a practical, low-cost surrogate marker for identifying patients entering the critical phase of dengue shock or organ dysfunction [2, 4, 8]. Clinically, transaminase elevations must be interpreted alongside hematocrit, platelet kinetics, hemodynamic parameters, and coagulation status. Severe transaminase elevations (>1000 U/L), clinical jaundice, or INR prolongation should alert clinicians to imminent acute liver failure and warrant prompt supportive therapy in high-dependency settings.

CONCLUSION

Hepatic dysfunction is highly prevalent in hospitalized dengue patients, characterized predominantly by early and marked AST elevation. Higher transaminase levels and synthetic dysfunction (hypoalbuminemia, INR prolongation) correlate directly with plasma leakage, bleeding manifestations, ICU admission, and clinical severity. Routine evaluation and serial monitoring of liver function tests are strongly recommended in dengue clinical management protocols to enable early risk stratification and timely intervention.

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