E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.02.53

Research Article

Hepatic Dysfunction in Dengue Virus Infection: Spectrum, Severity, and Prognostic Implications

Dr. Isha Kashyap[1], Dr. Shivani Dogra[2], Dr. Urvashi Andotra[3*]
[1]HOD & Consultant Pathologist Swastik Diagnostic Laboratory LLP, Jammu, Jammu & Kashmir 180001.
[2]Consultant Pathologist Swastik Diagnostic Laboratory LLP, Jammu, Jammu & Kashmir 180001.
[3*]Consultant Pathologist Swastik Diagnostic Laboratory LLP, Jammu, Jammu & Kashmir 180001.
Corresponding Author: Dr. Urvashi Andotra
Consultant Pathologist Swastik Diagnostic Laboratory LLP, Jammu, Jammu & Kashmir 180001.
Received: 06.05.26, Revised: 04.06.26, Accepted: 11.07.26

ABSTRACT
Background: Liver involvement is a well-recognised complication of dengue virus infection, yet its frequency, pattern, and relationship to disease severity remain incompletely characterised in adult populations from endemic regions. Objective: This retrospective study evaluated the nature and extent of hepatic biochemical disturbances across the clinical spectrum of dengue illness and identified markers associated with adverse outcomes. Methods: Records of 196 laboratory-confirmed adult dengue cases with complete liver function test (LFT) data were examined. Cases were categorised as dengue fever (DF), dengue haemorrhagic fever (DHF), and dengue shock syndrome (DSS) according to standard WHO criteria. Hepatic parameters assessed included serum bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), serum albumin, and the international normalised ratio (INR). Results: Elevated transaminases were the predominant abnormality, with AST and ALT exceeding the upper limit of normal in 95.4% and 91.8% of patients respectively. A disproportionate rise in AST relative to ALT was consistently observed (mean AST 328.4 ± 44.1 U/L vs. ALT 202.7 ± 29.5 U/L; p = 0.021). Hyperbilirubinaemia (22.1%), hypoalbuminaemia (27.6%), and elevated ALP (34.2%) were less frequent. Patients with DSS showed significantly greater derangement across all hepatic parameters versus DF patients. Bilirubin, ALT, and ALP were markedly elevated in the setting of haemorrhage, secondary infection, and among non-survivors. Conclusions: Transaminase elevation is near-universal in dengue infection, with preferential AST rise serving as an early diagnostic pointer. Hyperbilirubinaemia and elevated ALP and ALT are associated with haemorrhagic complications, re-infection, and mortality, suggesting their utility as prognostic biomarkers in dengue management.

Keywords: Dengue Fever, Liver Function Tests, Aspartate Aminotransferase, Alanine Aminotransferase, Hepatic Involvement, Prognostic Markers.

INTRODUCTION
Dengue infection, caused by a single-stranded positive-sense RNA virus belonging to the Flaviviridae family, remains one of the most prevalent vector-borne illnesses globally. Transmitted primarily by Aedes aegypti mosquitoes, the disease is endemic across tropical and subtropical belt regions spanning Southeast Asia, the Indian subcontinent, Latin America, and sub -Saharan Africa. An estimated 390 million dengue infections occur annually worldwide, of which approximately 96 million manifest clinically [1].

The clinical presentation of dengue spans a wide continuum, ranging from a self-limiting febrile illness to life-threatening dengue haemorrhagic fever and circulatory shock. While the haematological consequences of dengue, particularly thrombocytopaenia and plasma leakage, have been extensively documented, the involvement of the liver is increasingly recognised as a significant dimension of dengue pathophysiology [2,3].

Hepatic injury during dengue infection may arise through multiple mechanisms, including direct viral cytopathy, immune-mediated destruction of hepatocytes by activated cytotoxic T lymphocytes, ischaemic injury secondary to microcirculatory dysfunction, and adverse effects of medications administered during the febrile illness [4]. The resulting spectrum of liver dysfunction ranges from subclinical enzyme elevation to overt jaundice and, in rare instances, acute liver failure [5]. Transaminase abnormalities in dengue exhibit a distinctive pattern in which AST rises to a greater extent than ALT. This contrasts sharply with the pattern observed in classical viral hepatitis, where ALT typically predominates, and instead resembles the enzyme profile seen

in myocardial injury or alcoholic liver disease [6]. The probable explanation for this phenomenon lies in the fact that AST, unlike ALT, is not confined to hepatocytes but is also abundantly expressed in skeletal muscle, cardiac muscle, and circulating monocytes, the last of which are actively targeted during dengue viraemia [7].

While several institutional series have characterised liver involvement in dengue, large adult-focused studies from northern India remain limited. The present investigation was undertaken to quantify the frequency and magnitude of hepatic biochemical disturbances across all categories of dengue illness, to correlate these abnormalities with clinical outcomes, and to identify which liver parameters may have prognostic utility.

MATERIALS AND METHODS

Study Setting and Patient Population

This was a retrospective observational study conducted at Swastik Diagnostic Laboratory LLP, Jammu, Jammu & Kashmir, India, during an epidemic period spanning August to November 2021. All adult patients (age ≥ 18 years) presenting with acute febrile illness during this period were screened for dengue infection. Serological confirmation was performed using NS1 antigen rapid testing and IgM/IgG enzyme-linked immunosorbent assay (ELISA) (Standard Diagnostics, South Korea). Patients with a positive NS1 antigen or IgM antibody result were enrolled.

A total of 196 patients who had complete LFT data available at the time of admission were included in the final analysis. Patients with known pre-existing hepatic disease, concurrent hepatitis A, B, C, or E co-infection (tested in clinically suspected cases), or those who had received hepatotoxic medications prior to presentation, were excluded from analysis.

Clinical Classification

Enrolled patients were classified into three groups based on the 2009 WHO dengue classification:

(a) Dengue Without Warning Signs (DF group)
(b) (Dengue With Warning Signs / Dengue Haemorrhagic Fever (DHF group), and
(c) Severe Dengue / Dengue Shock Syndrome (DSS group). Secondary dengue infection was identified by the concurrent presence of both IgM and IgG antibodies (n = 38). Clinical outcomes were categorised as survivor and non-survivor.

Laboratory Assessment

Biochemical liver tests performed at admission included serum total bilirubin (mg/dL), AST (U/L), ALT (U/L), ALP (U/L), serum albumin (g/dL), and prothrombin time expressed as the INR. Normal reference ranges applied were: bilirubin ≤ 1.2 mg/dL; AST ≤ 40 U/L; ALT ≤ 40 U/L; ALP ≤ 120 U/L; albumin ≥ 3.5 g/dL; INR ≤ 1.2.

Statistical Analysis

Categorical variables are expressed as proportions and compared using the chi-square test or Fisher's exact test. Continuous variables are reported as mean ± standard error (SE). Between-group comparisons of means were performed using Student's unpaired t-test. A two-tailed p-value of < 0.05 was considered statistically significant. All analyses were performed using SPSS version 26.0 (IBM Corp., USA).

RESULTS

Patient Demographics and Clinical Classification

Among the 196 patients included, the majority were classified as DF (n = 158; 80.6%), followed by DHF (n = 27; 13.8%) and DSS (n = 11; 5.6%). Secondary dengue infection, indicated by dual IgM and IgG seropositivity, was identified in 38 patients (19.4%), with the highest proportion in the DSS group (70.4%; 8/11). The mean age was 29.8 years (range 18–74), and the male-to-female ratio was 2.9:1 (148 males, 48 females). The 21–30-year age bracket comprised the largest segment of patients (36.2%; n = 71).

Universal presenting symptoms included fever (100%). Myalgia was reported in 41.3% (n = 81), haemorrhagic manifestations in 38.8% (n = 76), nausea or vomiting in 35.2% (n = 69), and abdominal discomfort in 22.4% (n = 44). Physical examination at admission revealed hepatomegaly in 14.3% (n = 28), with a significantly higher prevalence in DSS (45.5%) than DF patients (11.4%; $p < 0.05$). Splenomegaly and ascites were each identified in approximately 2.0% of patients. Altered consciousness was recorded in four patients (2.0%).

Overall Biochemical Liver Profile

Hepatic biochemical derangements were highly prevalent (Table 1). AST exceeded the upper limit of normal in 95.4% (n = 187) of patients, and ALT in 91.8% (n = 180). Elevated ALP was found in 34.2% (n = 47/137), hypoalbuminaemia in 27.6% (n = 41/149),

hyperbilirubinaemia in 22.1% (n = 31/140), and a raised INR in 17.3% (n = 26/150).
The mean (± SE) values were: bilirubin 0.88 ± 0.08 mg/dL; AST 328.4 ± 44.1 U/L; ALT 202.7 ±
29.5 U/L; ALP 131.6 ± 7.2 U/L; albumin 3.3 ± 0.05 g/dL; INR 1.18 ± 0.03. The mean AST was significantly greater than the mean ALT value (p = 0.021), and a markedly higher proportion of patients demonstrated AST elevation exceeding ten times the upper limit of normal compared with ALT (p < 0.001).

Table1. Biochemical Hepatic Test Findings across the Dengue Illness Spectrum

Parameter	DF (n=158)	DHF (n=27)	DSS (n=11)	p*
Bilirubin (mg/dL) – mean ± SE	0.74 ± 0.07	0.92 ± 0.16	2.61 ± 0.91	0.0001
Bilirubin > ULN – No. (%)	17/118 (14.4%)	5/14 (35.7%)	9/11 (81.8%)	0.0001
AST (U/L) – mean ± SE	261.4 ± 19.8	462.1 ± 148.6	1198.3 ± 741.5	0.0001
AST > ULN – No. (%)	150/158 (94.9%)	27/27 (100%)	11/11 (100%)	1.000
ALT (U/L) – mean ± SE	162.3 ± 10.7	247.9 ± 72.4	796.4 ± 418.3	0.0001
ALT > ULN – No. (%)	145/158 (91.8%)	25/27 (92.6%)	11/11 (100%)	1.000
ALP (U/L) – mean ± SE	118.7 ± 5.1	161.4 ± 26.7	238.1 ± 58.9	0.0001
Albumin (g/dL) – mean ± SE	3.4 ± 0.05	3.1 ± 0.16	2.8 ± 0.19	0.0003
INR – mean ± SE	1.1 ± 0.02	1.2 ± 0.06	1.4 ± 0.12	0.012

*p value: DF vs. DSS comparison; DF = Dengue Fever, DHF = Dengue Haemorrhagic Fever, DSS = Dengue Shock Syndrome, ULN = Upper Limit of Normal

Comparison between Dengue Subgroups

All mean hepatic biochemical parameters were significantly more abnormal in the DSS subgroup compared with DF (p < 0.001 for bilirubin, AST, ALT, ALP, and albumin). Although the proportion of patients with abnormal transaminases was comparable across all three groups, the magnitude of elevation was substantially greater in DSS. Comparing DF with DHF, statistically significant differences were observed for mean AST (p = 0.016), ALP (p = 0.009), and albumin (p = 0.011), while the difference in bilirubin approached but did not reach significance

Liver Function and Clinical Subgroups

Patients with haemorrhagic manifestations (n = 76) demonstrated significantly higher mean bilirubin (1.09 ± 0.17 vs. 0.74 ± 0.07 mg/dL; p = 0.048), ALT (278.3 ± 59.1 vs. 162.1 ± 11.4 U/L; p = 0.031), and ALP (149.3 ± 12.8 vs. 119.2 ± 5.7 U/L; p = 0.018) than those without. This effect was amplified among patients with gastrointestinal haemorrhage specifically, where AST was additionally elevated to a significant degree (p = 0.019), perhaps reflecting concurrent ischaemic hepatic insult from acute blood loss.
Secondary dengue infection was associated with greater hepatic derangement. Patients with dual seropositivity (IgM + IgG) had significantly elevated mean bilirubin (1.74 ± 0.34 vs. 0.67 ± 0.05 mg/dL; p = 0.0001), ALT (318.2 ± 112.7 vs. 184.4 ± 16.3 U/L; p = 0.041), and ALP (169.3 ± 19.7
vs. 120.8 ± 6.1 U/L; p = 0.0008) compared with primary infection, consistent with enhanced immunopathological response during re-infection

Table 2. Hepatic Biochemical Values Stratified by Clinical Characteristics

Characteristic	Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	ALP (U/L)
Haemorrhage				
With haemorrhage (n=76)	1.09 ± 0.17	448.2 ± 111.4	278.3 ± 59.1	149.3 ± 12.8
Without haemorrhage (n=120)	0.74 ± 0.07	269.4 ± 23.6	162.1 ± 11.4	119.2 ± 5.7
p value	0.048	0.071	0.031	0.018
Primary vs. Secondary Infection				
IgM only (primary; n=158)	0.67 ± 0.05	298.6 ± 31.7	184.4 ± 16.3	120.8 ± 6.1
IgM + IgG (secondary; n=38)	1.74 ± 0.34	497.2 ± 53.9	318.2 ± 112.7	169.3 ± 19.7

p value	0.0001	0.101	0.041	0.0008
Outcome				
Survivors (n=190)	0.80 ± 0.07	322.1 ± 44.8	194.3 ± 26.7	125.7 ± 6.3
Characteristic	**Bilirubin (mg/dL)**	**AST (U/L)**	**ALT (U/L)**	**ALP (U/L)**
Non-survivors (n=6)	3.08 ± 1.54	448.7 ± 238.9	528.6 ± 361.4	236.4 ± 68.9
p value	0.0001	0.712	0.029	0.002

Liver Function and Outcomes

Mortality in this cohort was 3.1% (6/196). Causes of death included refractory shock (n = 2), acute respiratory distress syndrome (n = 2), severe disseminated intravascular coagulation with haemorrhage (n = 1), and underlying decompensated liver disease (n = 1). Non-survivors exhibited significantly elevated bilirubin, ALT, and ALP at admission compared with survivors (Table 2). AST, while numerically higher in non-survivors, did not reach significance (p = 0.712). There was no statistically significant difference in any hepatic parameter between male and female patients.

DISCUSSION

This investigation documents the hepatic biochemical profile of 196 adults with confirmed dengue infection admitted during a seasonal epidemic in northern India, reinforcing the understanding that liver involvement is among the most consistent and clinically important systemic manifestations of dengue disease.

Transaminase elevation was nearly universal in our cohort, occurring in more than 91% of patients regardless of dengue severity category. This observation aligns with previously published series from the Indian subcontinent and South-East Asia, which have similarly reported high rates of aminotransferase abnormality during dengue outbreaks [7,8,9]. Of particular note was the consistent dominance of AST over ALT, a pattern well documented in dengue infection but distinct from that of hepatotropic viral infections. This divergence may be explained by the broader tissue distribution of AST, which is released not only from injured hepatocytes but also from dengue-damaged monocytes, erythrocytes, and striated muscle cells [6,10]. The presence of AST elevation out of proportion to ALT early in the febrile course may thus serve as a useful early pointer toward dengue aetiology in a febrile patient.

Although the frequency of liver enzyme elevation was comparable across DF, DHF, and DSS subgroups, the severity of biochemical derangement escalated markedly with increasing clinical severity, mirroring findings reported by Seneviratne and colleagues [4]. In patients with DSS, all hepatic parameters were significantly worse, with AST exceeding 1000 U/L in several cases. This severity gradient suggests that the degree of hepatocellular injury is closely coupled to the haemodynamic compromise and systemic inflammatory response characteristic of severe dengue

The association between haemorrhage and worsening hepatic function deserves attention. Bilirubin, ALT, and ALP were significantly higher in patients with haemorrhagic manifestations, and the effect was most pronounced in those with gastrointestinal bleeding. A plausible mechanism is ischaemic hepatitis arising from acute blood loss and diminished hepatic perfusion, a well-recognised cause of dramatic transaminase elevation in other clinical contexts [11]. This finding underscores the importance of monitoring liver function closely in dengue patients who develop haemorrhage. Patients experiencing secondary dengue infection exhibited substantially greater hepatic biochemical disturbance across multiple parameters. This is consistent with the antibody-dependent enhancement hypothesis, whereby pre-existing, non-neutralising antibodies from a prior serotype facilitate greater viral entry into monocytes during re-infection, amplifying the inflammatory response and consequent organ injury [12]. The enhanced cytokine release associated with secondary infection likely drives more severe hepatocellular damage, as reflected in our data.

Hyperbilirubinaemia, though occurring in only a minority of patients overall, was strongly associated with adverse outcomes. Among non-survivors, mean serum bilirubin was nearly four times that of survivors. Jaundice in the context of dengue infection has been linked to fulminant hepatic failure in several case series and is generally regarded as an ominous clinical sign [5,13]. Our findings support this interpretation and suggest that clinicians should exercise heightened vigilance and consideration for intensive monitoring when bilirubin rises substantially in dengue patients.

The pattern of elevated ALP in severe dengue and non-survivors is also noteworthy, as ALP

elevation suggests involvement of the biliary epithelium or sinusoidal endothelium, in addition to hepatocyte injury. Whether this reflects direct viral targeting of non-parenchymal liver cells or a secondary consequence of haemodynamic stress merits further mechanistic investigation.

CONCLUSION

Biochemical evidence of hepatic involvement is nearly ubiquitous across all forms of dengue illness. The disproportionate elevation of AST relative to ALT represents a characteristic and early hepatic signature of dengue infection that may aid clinical differentiation from viral hepatitis in endemic settings. Serum bilirubin, ALT, and ALP are significantly elevated in patients with haemorrhage, secondary infection, severe dengue shock, and fatal outcomes, establishing their role as indicators of both disease severity and poor prognosis. Integration of liver function parameters into clinical risk stratification algorithms for dengue patients may help identify those requiring intensive monitoring and expedited management.

REFERENCES

1. Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. Nature. 2013; 496(7446): 504–507.
2. World Health Organization. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. New Edition. Geneva: WHO, 2009.
3. Rothman AL. Dengue: defining protective versus pathologic immunity. J Clin Invest. 2004; 113(7): 946–951.
4. Seneviratne SL, Malavige GN, de Silva HJ. Pathogenesis of liver involvement during dengue viral infections. Trans R Soc Trop Med Hyg. 2006; 100(8): 608–614.
5. Lum LC, Lam SK, George R, Devi S. Fulminant hepatitis in dengue infection. Southeast Asian J Trop Med Public Health. 1993; 24(3): 467–471.
6. Kuo CH, Tai DI, Chang-Chein CS, et al. Liver biochemical tests and dengue fever. Am J Trop Med Hyg. 1992; 47(3): 265–270.
7. Itha S, Kashyap R, Krishnani N, et al. Profile of liver involvement in dengue virus infection. Natl Med J India. 2005; 18(3): 127–130.
8. Daniel R, Rajamohanan, Philip AZ. A study of clinical profile of dengue fever in Kollam, Kerala, India. Dengue Bulletin. 2005; 29: 197–202.
9. Souza LJ, Alves JG, Nogueira RM, et al. Aminotransferase changes and acute hepatitis in patients with dengue fever: analysis of 1,585 cases. Braz J Infect Dis. 2004; 8(2): 156–163.
10. Kalayanarooj S, Vaughn DW, Nimmannitya S, et al. Early clinical and laboratory indicators of acute dengue illness. J Infect Dis. 1997; 176(2): 313–321.
11. Henrion J. Hypoxic hepatitis. Liver Int. 2012; 32(7): 1039–1052.
12. Halstead SB. Dengue antibody-dependent enhancement: knowns and unknowns. Microbiol Spectr. 2014; 2(6): AID-0022-2014.
13. Nguyen TL, Nguyen NT, Tieu NT. The impact of dengue fever on liver function. Res Virol. 1997; 148(4): 273–277