Journal of Advanced Scientific Research

Available online through https://sciensage.info

ISSN

0976-9595

Research Article

Prospective Evaluation of Hepatic Dysfunction in Patients with Dengue Fever: A Clinical and Biochemical Outcome Study

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Received: 10-04-2026; Accepted: 24-05-2026; Published: 30-05-2026

 https://doi.org/10.55218/JASR.2026170509

ABSTRACT

Background: Dengue fever is a rapidly emerging mosquito-borne viral illness with a wide clinical spectrum ranging from mild febrile disease to severe life-threatening complications. Hepatic dysfunction is increasingly recognized as a significant systemic manifestation of dengue infection and may serve as an early predictor of disease severity and adverse clinical outcomes. However, prospective data from eastern India, particularly Bihar, remain limited.

Aim: To prospectively evaluate the clinical profile and biochemical pattern of hepatic dysfunction in patients with dengue fever and determine its association with disease severity and clinical outcomes in a tertiary care center in Bihar.

Methodology: This prospective observational study included 120 adult patients with laboratory-confirmed dengue infection selected randomly from those presenting to the outpatient department over a six-month period. Detailed clinical evaluation and laboratory investigations, including liver function tests (AST, ALT, bilirubin, albumin, and coagulation profile) were performed. Hepatic dysfunction was assessed and correlated with the WHO dengue severity classification and clinical outcomes. Statistical analysis was performed using SPSS version 20.0, with $p < 0.05$ considered significant.

Results: Elevated AST and ALT were observed in 85% and 78.3% of patients, respectively, with AST levels exceeding ALT. Hyperbilirubinemia and hypoalbuminemia were noted in 22.5 and 28.3% of cases. Significant association was found between hepatic dysfunction and severity of dengue ($p < 0.05$). Patients with severe dengue had markedly elevated transaminases, longer hospital stay, and higher ICU admission rates. Mortality was observed in 1.7% of cases, all associated with severe hepatic involvement.

Conclusion: Hepatic dysfunction is highly prevalent in dengue fever and strongly correlates with disease severity and outcomes. Routine liver function assessment is a valuable, cost-effective prognostic tool for early identification of high-risk patients in tertiary care settings.

Keywords: Dengue, Hepatic dysfunction, Liver function tests, Transaminases, Disease severity.

INTRODUCTION

Dengue fever is one of the most rapidly spreading mosquito-borne viral diseases globally, posing a major public health challenge in tropical and subtropical regions, particularly in Southeast Asia and India. The disease is caused by four serotypes of the dengue virus (DENV 1–4) transmitted by *Aedes aegypti* mosquitoes and presents with a wide clinical spectrum ranging from asymptomatic infection and mild febrile illness to severe dengue characterized by plasma leakage, hemorrhage, shock, and multi-organ dysfunction [1]. Among the organs affected, the liver is one of the most commonly involved, with hepatic dysfunction being increasingly recognized as an important component of dengue pathophysiology and a determinant of disease severity [2].

Hepatic involvement in dengue is multifactorial and results from a combination of direct viral cytopathic effects, immune-mediated injury, and hypoxic damage due to circulatory compromise [3]. Several studies have shown that the dengue virus can infect hepatocytes and Kupffer cells, leading to inflammatory cytokine release, hepatocellular injury, and disruption of hepatic metabolic functions [3]. Elevated liver enzymes, particularly aspartate transaminase (AST) and alanine transaminase (ALT), are commonly observed in dengue patients, often with AST levels exceeding ALT levels, reflecting both hepatic and extrahepatic tissue injury [4].

Clinical manifestations of hepatic involvement in dengue range from asymptomatic transaminase elevation to acute hepatitis, jaundice, hepatomegaly, coagulopathy, and rarely, fulminant hepatic failure [5]. Studies indicate that elevated AST and ALT levels are present in up to 80 to 90% of dengue patients and are more pronounced in severe dengue, dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) [6]. In addition, abnormal liver function parameters such as hypoalbuminemia, prolonged prothrombin time, and hyperbilirubinemia have been associated

with poor clinical outcomes, prolonged hospital stay, and increased mortality [7].

Recent evidence has highlighted the prognostic significance of hepatic dysfunction in dengue. Elevated transaminase levels correlate strongly with disease severity, risk of complications, and need for intensive care [6]. Studies have demonstrated that AST levels, in particular, may serve as early markers for identifying severe dengue cases and guiding risk stratification [6]. Furthermore, hepatic dysfunction has been associated with immune activation markers such as interleukins and endothelial dysfunction, suggesting that liver injury in dengue may reflect systemic inflammatory and vascular processes [8]. Therefore, monitoring hepatic parameters is crucial not only for diagnosis but also for early prediction of disease progression.

India bears a substantial burden of dengue cases, with recurrent outbreaks reported from various states, including Bihar. The state of Bihar, located in eastern India, experiences seasonal dengue epidemics, particularly during and after the monsoon period, due to favorable climatic conditions for mosquito breeding, inadequate sanitation, and dense population clusters. Government medical colleges in bihar serve as major referral and teriary care centers for patients from both urban and rural areas, often managing complicated and severe dengue cases. These centers receive a high load of patients with advanced disease due to delayed referral, lack of early diagnosis, and limited healthcare access in peripheral regions.

Despite the high burden of dengue in Bihar, there is a paucity of region-specific prospective studies evaluating hepatic dysfunction and its clinical outcomes in dengue patients. Most available studies are retrospective or conducted in other geographic regions, and their findings may not be directly applicable to the local population due to differences in viral serotypes, host factors, nutritional status, comorbidities, and healthcare infrastructure. Additionally, the pattern of hepatic involvement may vary based on demographic and environmental factors, making it essential to conduct localized prospective research.

A government medical college in Bihar provides an ideal setting for such a study, as it caters to a diverse patient population and acts as a referral hub for severe and complicated dengue cases. Prospective evaluation in such a setting allows for systematic assessment of clinical features, biochemical parameters, and outcomes, thereby enabling better understanding of disease patterns and improving patient management strategies. Early identification of hepatic dysfunction in dengue patients can help clinicians initiate timely interventions, prevent complications, and reduce mortality.

Furthermore, understanding the biochemical profile of liver dysfunction in dengue can contribute to the development of simple, cost-effective prognostic markers that can be used even in resource-limited settings. This is particularly relevant for Bihar, where healthcare resources are limited and early risk stratification can significantly improve patient outcomes. Such evidence can also support public health planning, resource allocation, and the development of clinical guidelines tailored to the regional population.

There is a significant need to evaluate hepatic dysfunction in dengue patients in Bihar due to:

High disease burden and seasonal outbreaks in the region. Limited prospective data on hepatic involvement in dengue from Bihar. Increasing recognition of liver dysfunction as a prognostic indicator of severe dengue. Role of tertiary care centers as referral hubs for complicated cases. Need for early identification of high-risk patients to reduce morbidity and mortality.

The present study aims to prospectively evaluate the clinical profile and biochemical pattern of hepatic dysfunction in patients with dengue fever admitted to a tertiary care center in Bihar and to determine its association with disease severity and clinical outcomes.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of General Medicine at Jannayak Karpoori Thakur Medical College and Hospital in Bihar, India, which is a government medical college serving as a major referral center for patients from both urban and rural regions of the state. The hospital caters to a large patient population and receives a high volume of dengue cases, particularly during the monsoon and post-monsoon seasons when vector breeding is at its peak. The study was carried out over a period of six months from July 2025 to December 2025, corresponding to the seasonal surge of dengue infection in the region. The tertiary care setting enabled comprehensive clinical evaluation, laboratory investigations, and monitoring of disease progression and outcomes in admitted as well as outpatient cases.

The present study was designed as a prospective observational cohort study aimed at evaluating hepatic dysfunction in patients diagnosed with dengue fever. All eligible patients presenting to the outpatient department (OPD) and subsequently requiring admission or observation were randomly selected and enrolled after obtaining informed consent. The study followed a longitudinal approach, where patients were assessed at baseline (time of presentation) and monitored throughout the course of illness until discharge or clinical recovery. The design allowed for systematic documentation of clinical features, biochemical liver function parameters, and outcome measures.

The study population consisted of patients diagnosed with dengue fever attending the OPD or admitted to the medicine wards of the tertiary care hospital. The sample size was determined based on feasibility and expected patient load during the dengue season. Over the six-month study period, a total of 120 patients fulfilling the eligibility criteria were randomly selected from among those presenting to the OPD with suspected dengue infection and subsequently confirmed by laboratory testing. Random selection was carried out using a simple random sampling method from the daily case list of laboratory-confirmed dengue patients to minimize selection bias and ensure representative sampling.

Inclusion Criteria

Patients were included in the study if they met the following criteria: Age ≥18 years, of either sex. Laboratory-confirmed dengue infection, diagnosed by positive NS1 antigen and/or dengue IgM antibody test. Patients presenting within 7 days of the onset of fever. Patients willing to provide informed written consent for participation in the study. Patients available for follow-up during the hospital stay or observation period.

Exclusion Criteria

Patients were excluded from the study under the following conditions: Known cases of **chronic liver disease** (cirrhosis, chronic hepatitis

B or C infection). History of alcoholic liver disease or significant alcohol intake. Patients with co-infections known to affect liver function (such as malaria, leptospirosis, typhoid fever, viral hepatitis A/E). Patients taking hepatotoxic drugs (e.g., antitubercular therapy, chemotherapy). Pregnant women. Patients with known metabolic or autoimmune liver disorders. Patients unwilling to participate or do not provide consent.

METHODOLOGY

All enrolled patients underwent a detailed clinical evaluation at the time of admission or OPD presentation. A structured proforma was used to record demographic details (age, sex, residence), clinical symptoms (fever, headache, myalgia, abdominal pain, nausea, vomiting, bleeding manifestations), and duration of illness. A thorough general and systemic examination was performed with special attention to hepatomegaly, jaundice, ascites, bleeding manifestations, and hemodynamic status. Disease severity was classified according to the WHO dengue guidelines into dengue fever, dengue with warning signs, and severe dengue.

Baseline laboratory investigations were performed at admission and repeated as clinically indicated during the hospital stay. The following investigations were included: Complete blood count (hemoglobin, total leukocyte count, platelet count), Hematocrit, Liver function tests (AST, ALT, alkaline phosphatase, total bilirubin, direct bilirubin, serum albumin), Coagulation profile (prothrombin time, INR), Renal function tests (blood urea, serum creatinine), Dengue serology (NS1 antigen, IgM antibody), All biochemical tests were performed using standardized automated analyzers in the central laboratory of the institution.

Hepatic dysfunction was defined based on abnormal liver function parameters, including: Elevation of AST and/or ALT above the upper limit of normal, Hyperbilirubinemia (>1.2 mg/dL), Hypoalbuminemia (<3.5 g/dL), Prolonged prothrombin time/INR.

Severity of liver involvement was graded as mild (1-2 times elevation of enzymes), moderate (2–5 times), and severe (>5 times elevation). Patients were monitored for the development of acute hepatitis, liver failure, or other complications.

The primary outcome was the pattern and severity of hepatic dysfunction in dengue patients. Secondary outcomes included: Association between liver dysfunction and disease severity. Duration of hospital stay. Need for intensive care or supportive interventions. Occurrence of complications such as bleeding, shock, or multi-organ dysfunction. Clinical recovery or mortality.

Data collected from all enrolled patients were entered into a Microsoft Excel spreadsheet and analyzed using Statistical Package for the Social Sciences (SPSS) version 20.0. Continuous variables such as age, liver enzyme levels, and laboratory parameters were expressed as mean ± standard deviation (SD). Categorical variables such as gender, clinical features, and severity categories were expressed as frequencies and percentages. The Chi-square test was used for categorical variables, while the Student's t-test was used for continuous variables. One-way ANOVA was applied for comparison across multiple severity groups. A *p-value* of <0.05 was considered statistically significant.

RESULTS

A total of 120 laboratory-confirmed dengue patients were included in this prospective study conducted over a period of six months. All patients were evaluated for clinical features, hematological parameters, and hepatic function, and their outcomes were recorded.

The mean age of the study population was 34.6 ± 12.8 years, with the majority of patients belonging to the 21–40 years age group (48.3%). There was a male predominance (60%), with a male-to-female ratio of 1.5:1. Most patients (65%) were from rural areas, reflecting the referral pattern of the tertiary care center.

The majority of dengue patients were young adults, with male predominance and a higher representation of rural populations, indicating possible exposure and referral bias to the tertiary care center.

Fever was present in 100% of patients, followed by myalgia (76.7%), headache (68.3%), and vomiting (41.7%). Hepatomegaly was noted in 30% of patients, while jaundice was observed in 12.5%. According to WHO classification, 66.7% had uncomplicated dengue, 25% had dengue with warning signs, and 8.3% had severe dengue.

Hepatic involvement was clinically evident in a significant proportion of patients, with hepatomegaly and jaundice being

Table 1: Demographic characteristics of study population (n = 120)

Variable	*Frequency*	*Percentage (%)*
Age group (years)		
18–20	14	11.7
21–40	58	48.3
41–60	32	26.7
>60	16	13.3
Gender		
Male	72	60.0
Female	48	40.0
Residence		
Rural	78	65.0
Urban	42	35.0

Table 2: Clinical features and severity classification

Clinical feature	*Frequency (n)*	*Percentage (%)*
Fever	120	100
Myalgia	92	76.7
Headache	82	68.3
Vomiting	50	41.7
Abdominal pain	44	36.7
Bleeding manifestations	18	15.0
Hepatomegaly	36	30.0
Jaundice	15	12.5
Severity Category		
Dengue fever	80	66.7
Dengue with warning signs	30	25.0
Severe dengue	10	8.3

Table 3: Liver function parameters in dengue patients

Parameter	*Mean ± SD*	*Abnormal n (%)*
AST (IU/L)	146.5 ± 82.4	102 (85.0%)
ALT (IU/L)	112.8 ± 64.7	94 (78.3%)
Total Bilirubin (mg/dL)	1.4 ± 0.8	27 (22.5%)
Serum Albumin (g/dL)	3.2 ± 0.6	34 (28.3%)
Prothrombin Time (sec prolonged)	—	18 (15.0%)

important indicators of liver dysfunction. Severe dengue was present in a smaller but clinically significant group.

Liver function abnormalities were observed in the majority of patients. Elevated AST was seen in 85%, while ALT elevation was noted in 78.3%. The mean AST level was 146.5 ± 82.4 IU/L, and the mean ALT level was 112.8 ± 64.7 IU/L. Hyperbilirubinemia was present in 22.5%, and hypoalbuminemia in 28.3% of patients.

The most frequent hepatic abnormality was elevation of transaminases, particularly AST, followed by ALT. Other indicators, such as bilirubin elevation and hypoalbuminemia, were associated with more severe disease.

A statistically significant association was found between the degree of liver enzyme elevation and the severity of dengue ($p < 0.05$). Patients with severe dengue had markedly elevated AST/ALT levels compared to those with uncomplicated dengue. The mean hospital stay was 6.8 ± 2.4 days, which was significantly longer in patients with severe hepatic dysfunction.

The table clearly demonstrates that increasing levels of hepatic dysfunction were significantly associated with severe dengue, longer hospitalization, and higher ICU admission rates. Elevated AST and ALT levels were strong predictors of disease severity.

Out of 120 patients, 112 (93.3%) recovered completely, while 8 patients (6.7%) required ICU care. Mortality was observed in 2 patients (1.7%), both of whom had severe dengue with marked hepatic dysfunction and multi-organ involvement.

DISCUSSION

The present prospective study evaluated hepatic dysfunction in patients with dengue fever admitted to a tertiary care center in Bihar and demonstrated that liver involvement is highly prevalent and significantly associated with disease severity and clinical outcomes. The findings of this study are consistent with the growing body of evidence that hepatic dysfunction is a key systemic manifestation of dengue infection and a useful prognostic marker for identifying severe disease [1].

In the current study, elevated transaminases were observed in the majority of patients, with AST elevation (85%) being more frequent than ALT elevation (78.3%). This pattern has been consistently reported in previous studies, where AST tends to be disproportionately elevated due to its release not only from hepatocytes but also from myocytes and erythrocytes during systemic viral infection [1,2]. Trung et al. demonstrated that AST predominance is a characteristic biochemical feature of dengue-related liver injury and reflects the multisystem involvement of the disease [2]. Similar findings were reported in studies from India and Southeast Asia, which observed elevated AST levels in 70–90% of dengue patients, with significantly higher levels in severe dengue cases [3,4].

The mean AST and ALT levels in the present study were significantly higher in patients with severe dengue compared to those with uncomplicated dengue, showing a strong statistical association ($p < 0.001$). This supports previous observations that transaminase levels correlate positively with disease severity, plasma leakage, and risk of complications [5]. Srisawat et al. reported that elevated liver enzymes are closely linked to endothelial activation and cytokine-mediated inflammation, which are central to dengue pathogenesis [6]. Therefore, liver dysfunction may be considered not only an organ-specific manifestation but also a surrogate marker of systemic inflammatory response.

Hyperbilirubinemia was observed in 22.5% of patients in this study and was significantly higher in severe dengue cases. This finding is comparable to the results of Das et al., who reported bilirubin elevation in 20–30% of hospitalized dengue patients and found it to be associated with prolonged hospital stay and adverse outcomes [7]. Although jaundice is less common than transaminase elevation, its presence indicates more severe hepatocellular injury or cholestasis and warrants closer monitoring.

Hypoalbuminemia was observed in 28.3% of patients and was significantly associated with severe dengue and longer hospital stay. This finding reflects increased vascular permeability and plasma leakage, which are hallmarks of severe dengue infection [5,6]. Rahman et al. similarly reported that low serum albumin levels correlate with disease severity and can serve as an early predictor of complications [8]. In resource-limited settings like Bihar, serum albumin measurement can be a simple and cost-effective tool for risk stratification.

In the present study, hepatomegaly was observed in 30% of patients, which is comparable to previous studies reporting hepatomegaly in 20–40% of dengue cases [3,5]. The presence of hepatomegaly indicates inflammatory involvement of the liver and is often associated with elevated liver enzymes. Clinical signs such as hepatomegaly and jaundice, although less sensitive than

Table 4: Association of hepatic dysfunction with disease severity and outcome

Parameter	*Mild dengue (n=80)*	*Warning signs (n=30)*	*Severe dengue (n=10)*	*p-value*
Mean AST (IU/L)	102.3 ± 45.6	178.4 ± 70.2	312.6 ± 96.8	<0.001
Mean ALT (IU/L)	88.5 ± 40.1	134.2 ± 56.7	256.3 ± 80.5	<0.001
Hyperbilirubinemia (%)	10.0	30.0	70.0	<0.01
Mean hospital stay (days)	5.2 ± 1.6	7.4 ± 2.1	10.6 ± 3.2	<0.01
ICU admission (%)	0	10.0	60.0	<0.001

biochemical parameters, remain important bedside indicators of hepatic involvement.

The association between hepatic dysfunction and clinical outcomes was clearly demonstrated in this study. Patients with higher transaminase levels and bilirubin had significantly longer hospital stays, increased need for intensive care, and higher risk of complications. These findings are in agreement with those of Wagle et al., who showed that liver enzyme elevation is a strong predictor of ICU admission and severe dengue [9]. Similarly, Ahmed et al. observed that patients with AST levels greater than five times the upper limit of normal had significantly higher morbidity and mortality [5].

The mortality rate in this study was 1.7%, and all deaths occurred in patients with severe dengue and marked hepatic dysfunction, highlighting the role of liver involvement as a marker of poor prognosis. Although fulminant hepatic failure is rare in dengue, when it occurs, it is associated with high mortality and requires aggressive supportive management [4,9].

An important strength of this study is its prospective design and its conduct in a tertiary care referral center in Bihar, which allowed systematic evaluation of patients from diverse socioeconomic and geographic backgrounds. The findings are particularly relevant to eastern India, where dengue incidence is rising and healthcare resources are limited. Early identification of hepatic dysfunction in such settings can help clinicians prioritize high-risk patients and optimize resource utilization.

However, certain limitations must be acknowledged. The study was conducted at a single center with a relatively limited sample size, which may affect generalizability. Viral serotyping and advanced immunological markers were not assessed due to resource constraints. Despite these limitations, the study provides valuable insight into the clinical and biochemical spectrum of hepatic involvement in dengue fever in a high-burden region.

CONCLUSION

The present study confirms that hepatic dysfunction is a common and clinically significant manifestation of dengue fever and is strongly associated with disease severity and outcomes. Routine assessment of liver function tests, particularly AST, ALT, bilirubin, and albumin, can serve as valuable prognostic tools in the management of dengue patients. Early detection of hepatic involvement can facilitate timely intervention, reduce complications, and improve patient outcomes, especially in resource-constrained tertiary care settings in Bihar.

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HOW TO CITE THIS ARTICLE: Kumar V, Gupta JP, Jha AK, Kumar B. Prospective Evaluation of Hepatic Dysfunction in Patients with Dengue Fever: A Clinical and Biochemical Outcome Study. *J Adv Sci Res*. 2026;17(5): 41-45 **DOI:** 10.55218/JASR.2026170509