

# Patterns of Liver Function Test Derangement in Dengue Fever and Dengue Hemorrhagic Fever

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## Author's Contribution

<sup>1-4</sup> Substantial contributions to the conception or design of the work; or the acquisition, Drafting the work or revising it critically for important intellectual content  
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## ABSTRACT

**Objective:** To identify and contrast the patterns of liver function test abnormalities in patients admitted to a tertiary care hospital with dengue fever (DF) and dengue hemorrhagic fever (DHF), a cross-sectional research was carried out.

**Methodology:** This observational cross-section study was conducted at Jinnah Hospital, Lahore, from March to August 2025. The study included 100 individuals with confirmed dengue infection (NS1 antigen or IgM positive). Both clinical characteristics and laboratory results were documented, such as total bilirubin levels, aspartate aminotransferase (AST), and alanine aminotransferase (ALT). Data were analyzed using SPSS version 27. The association between liver function abnormalities and dengue fever and dengue hemorrhagic fever was assessed using chi-square tests.

**Results:** Elevated ALT levels were observed in 28% of patients with dengue fever (DF), 11% of patients with DF with hemorrhage, and 61% of patients with dengue hemorrhagic fever (DHF). A significant correlation was found between disease severity and elevated AST levels, which were observed in 26%, 11%, and 63% of patients, respectively. Elevated total bilirubin levels were noted in 8% of DF patients, 17% of DF with hemorrhage patients, and 75% of DHF patients. Painful hepatomegaly was present in 22% of patients, while 32% experienced active vomiting. A statistically significant association was observed between disease severity and elevated ALT, AST, and bilirubin levels ( $p = 0.001$ ).

**Conclusion:** Dengue infection frequently results in impaired liver function, especially in DHF. AST elevation may be a helpful indicator of hepatic involvement and was substantially correlated with the severity of the illness. The majority of abnormalities were minor and reversible, highlighting the significance of regular monitoring of liver function in dengue patients.

**Keywords:** Dengue Fever (DF), Severe Dengue, Liver function tests, Aspartate aminotransferase, Alanine aminotransferase

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## Introduction

Dengue fever is the world's fastest growing mosquito-borne viral illness and remains a major public health concern in tropical and subtropical countries. According to the WHO, there are around 390 million dengue infections each year, with Asia and South America accounting for over 70% of the disease burden<sup>1</sup>. Dengue

infection can range from a simple febrile sickness to severe types characterized by plasma leakage, hemorrhage, and shock. Along with the usual symptoms of fever, headache, retro-orbital discomfort, and myalgia, hepatic involvement is now well acknowledged as an important component of dengue pathogenesis.<sup>2</sup> Hepatic dysfunction in dengue may present as asymptomatic elevation of transaminases, hepatomegaly, jaundice, or,

rarely, acute liver failure. The underlying mechanisms are multifactorial and include direct viral cytopathic effects, immune-mediated hepatocyte injury, cytokine storms, hypoxic injury secondary to shock, and drug-induced hepatotoxicity. A characteristic pattern of dengue infection is a disproportionate elevation of AST compared to ALT, possibly reflecting concomitant muscle involvement.<sup>4</sup>

Many regional and international studies have shown a strong connection between disease severity and liver enzyme derangement. Several studies from Pakistan and Bangladesh have reported higher levels of transaminases (AST, ALT) and bilirubin among patients with DHF and those experiencing bleeding manifestations.<sup>5-7</sup> Both the adults and the pediatric data favors the relationship between elevated liver enzymes and thrombocytopenia, plasma leakage, and prolonged hospital stay.<sup>8-9</sup> A recent systematic review showed that elevated AST, ALT, bilirubin, hypoalbuminemia and coagulopathy are common in dengue-associated liver involvement and closely associated with severe dengue and multi-organ dysfunction.<sup>10</sup> Multiple recent hospital-based studies from Pakistan, India, Bangladesh and Nepal demonstrate that abnormal liver function tests (LFTs) are highly prevalent in dengue and correlate with severe dengue, DSS, ICU admission and mortality. Elevated AST and ALT, alone or in combination and rising bilirubin consistently show strong associations with severe disease and death, suggesting important prognostic value.<sup>11-14</sup>

Understanding of these patterns is vital for the early recognition of severe disease, appropriate monitoring, and improved clinical outcomes. Therefore, this study was conducted to evaluate and compare liver function test derangements among patients with dengue fever and dengue hemorrhagic fever admitted to a tertiary care hospital in Lahore. Given the high dengue burden in Lahore, the frequency of hepatic involvement, and the growing but still inconsistent literature on AST/ALT and bilirubin as markers of severity, there is a clear need to characterize the pattern and frequency of LFT derangements across DF or DHF in this specific setting.

By systematically comparing ALT, AST, and total bilirubin abnormalities between these clinical categories in admitted patients without pre-existing liver disease, this study aims to: Monitor the burden of hepatic dysfunction in hospitalized dengue patients at a major tertiary hospital in Lahore. Determine whether specific raised LFT abnormalities, particularly AST elevation, are associated with progression from DF to DHF, supporting

their use in early risk stratification, as suggested by recent regional and international evidence.

## Methodology

This is an observational cross-sectional conducted at the Department of Medicine, Jinnah Hospital, Lahore, from March to August 2025. A total of 100 patients with confirmed dengue infection were enrolled using non-probability consecutive sampling method. A prior approval was taken from the Ethical Review Committee [Ref No. 341/20/10/2022/S1 ERB] of Jinnah Hospital, Lahore. Patient confidentiality was strictly maintained.

Despite this developing data, reported patterns of LFT derangement (AST vs ALT predominance, bilirubin frequency, and thresholds utilized) vary significantly between geographical locations and classifications (traditional DF/DHF/DSS versus WHO 2009). Recent South Asian studies have typically included all severity groups or concentrated on "severe dengue" vs. "non-severe" without clearly distinguishing DF, DSS, and DHF, and there is minimal recent data from Lahore-based tertiary hospitals utilizing standardized, frequently accessible LFT parameters.<sup>11-15</sup>

Patients of either sex aged  $\geq 14$  years with laboratory-confirmed dengue infection (NS1 antigen or dengue IgM positive) were included in the study. Patients with known chronic liver disease, viral hepatitis, alcoholic liver disease, Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), autoimmune hepatitis, or concurrent systemic infections were excluded to avoid confounding effects on liver function tests.

The sample size was calculated as 92 using a 95% confidence interval and 8% margin of error, assuming an 81.2% prevalence of raised ALT based on previous literature.<sup>9</sup> A higher number of participants was enrolled to improve the study power.

Relevant clinical finding including symptoms, bleeding manifestations, and physical examination such as hepatomegaly, were recorded. Laboratory parameters, including Alanine aminotransferase/Serum glutamic-pyruvic transaminase (ALT/SGPT), Aspartate aminotransferase /Serum glutamic-oxaloacetic transaminase (AST/SGOT), and total bilirubin levels, were measured using standard automated analyzers.

Data were entered and analyzed using the IBM SPSS version 27. Qualitative variables were expressed as frequency and percentage. The association between liver function abnormalities and dengue fever and dengue

hemorrhagic fever was assessed using chi-square tests. Ethical approval was obtained from the Institutional Review Board of Jinnah Hospital, Lahore. A Chi square test was applied between Observed and Expected values of the Liver function tests' parameters between the groups. Another Chi Square test was applied between Dengue Severity and including cases of Dengue Hemorrhage cases with Dengue cases with Mucousal Bleeding. Statistical significance was set at  $p \leq 0.05$ .

## Results

The patients' ages were between 19-65 years. The mean age of the patients was  $40.7 \pm 1.41$  years. Among them, there were 55 male and 45 female patients. Among the 100 enrolled patients, liver enzyme abnormalities were observed with increasing frequency as the disease severity progressed from DF to DHF. In the present study, hepatomegaly was observed in 22.1% of patients, whereas bilirubin elevation was predominantly observed in DHF cases. Regarding clinical features, active vomiting was reported in 32% of patients, and tender hepatomegaly was detected in 22% of patients.

Elevation of ALT was noted in 28% of patients with DF, 11% of patients with DF with bleeding manifestations, and 61% of patients with DHF ( $p$  value  $< 0.05$ ). In contrast, AST elevation was significantly associated with disease severity, being present in 26% of DF, 11% of DF with bleeding, and 63% of DHF patients ( $p$  value  $< 0.05$ ). (Table I)

Elevated total bilirubin levels were observed in 8% of DF, 17% of DF with bleeding, and 75% of DHF patients ( $p$  value  $< 0.05$ ). Most patients demonstrated a gradual normalization of liver enzymes during recovery. Another Chi Square test was conducted with contingency table to compare the ALT/AST/Bilirubin's raised values with cases of Dengue severity. There existed a significant association with DF with the Disease Severity Cases

(DFMB + DHF) ( $p$  value = 0.001) for elevated levels of ALT/AST/Bilirubin (Table II). Among the study participants, active vomiting was observed in 32% of patients, while tender hepatomegaly was present in 22% of patients.

## Discussion

Studies have found that AST levels are elevated in 63-97% of cases while ALT levels are up in 45-96% of cases, with AST being the more common. In our investigation, elevated AST levels were shown to be significantly associated with DHF, indicating more severe hepatic and systemic involvement. Higher AST levels may indicate both hepatic inflammation and muscle damage, which is typical in dengue illness. Hyperbilirubinemia and hepatomegaly have reported rates ranging from 4% to 52%.<sup>12-20</sup> Hepatomegaly was seen in 22.1% of patients, while bilirubin increase was most common in DHF cases. None of the patients experienced fulminant hepatic failure, and liver enzyme abnormalities were transitory and reversible. These data support the view that dengue-induced hepatic dysfunction is mostly immune-mediated and self-limiting, rather than a primary hepatotropic viral damage.<sup>4-7</sup>

This study demonstrates that hepatic involvement is common among patients with dengue infection, with a clear gradient of liver dysfunction across DF, DF with bleeding, and DHF. The markedly higher proportion of AST elevation in DHF compared with DF and DF with bleeding, and its statistically significant association with disease severity, reinforces the role of AST as a potential early biomarker of severe dengue. Similar findings have been reported from recent multi-center and regional studies, where AST abnormalities were more frequent and pronounced than ALT in severe dengue and dengue with warning signs, and independently predicted progression to severe disease.<sup>21-23</sup> Nepal also identified

**Table I: Liver Function Abnormalities According to Disease Severity. (n = 100)**

Parameter	Mean Values	DF (n, %)	DF with Mucosal Bleeding -DFMB (n, %)	Dengue Hemorrhage Fever-DHF (n, %)
Elevated ALT	86.63 $\pm$ 5.987 (U/L)	28(28%)	11(11%)	61(61%)
Elevated AST	91.96 $\pm$ 6.275 (U/L)	26(36%)	11(11%)	63(63%)
Raised Bilirubin	1.4857 $\pm$ 0.0807 (mg/dl)	8(8%)	17(17%)	75(75%)

**Table II: Chi Square test to find significance between Dengue Fever cases with Dengue Severity Cases\*. (n = 100)**

Parameter	DF (n)	Disease Severity Cases* (n)	Chi Square Value	p-value
Elevated ALT	28	72	14.8	
Elevated AST	26	74		0.001**
Raised Bilirubin	8	92		

\*Dengue Severity was taken by including cases of Dengue Hemorrhage cases with Dengue cases with Mucousal Bleeding.

\*\*Statistically significant ( $p < 0.05$ ).

elevated AST, but not ALT, as an independent predictor of dengue with warning signs, with significant correlations with gastrointestinal symptoms and lower platelet counts, supporting the diagnostic and prognostic utility of AST in risk stratification.<sup>21</sup>

The frequency and pattern of liver enzyme abnormalities in the present cohort are broadly consistent with contemporary data from South and East Asia. Recent hospital-based studies from Pakistan, India, Bangladesh, Nepal, and China have reported hepatic dysfunction in 40–80% of dengue patients, with AST more commonly elevated than ALT and with higher levels in patients with severe dengue or DHF/DSS.<sup>24-30</sup> In a study from Rawalpindi, all major LFT parameters, including ALT, bilirubin, and albumin, correlated significantly with WHO-defined disease severity, and severity of hepatic impairment was associated with severe dengue.<sup>8</sup>

Similarly, studies from Multan, Kolkata, and coastal India have shown that higher transaminase and bilirubin levels are linked to DSS, hemorrhagic manifestations, ICU admission, and mortality, underscoring their prognostic value.<sup>25-31</sup> A 2025 emergency-department series also found that AST predominance and rising bilirubin were strongly associated with WHO 2009 severe dengue categories, echoing the pattern observed in DHF in the present study.<sup>32</sup>

The observation that most derangements in this cohort were mild and reversible aligns with previous descriptions of dengue-associated hepatitis as typically self-limited, with transaminases peaking around day 5–7 and normalizing within 2–3 weeks.<sup>24-25</sup> Nonetheless, severe hepatic injury and acute liver failure, although rare, carry substantial mortality. Recent cross-sectional and retrospective analyses emphasize that even moderate elevations of AST and ALT, particularly when combined (e.g., AST+ALT >300 U/L) or accompanied by hyperbilirubinemia and hypoalbuminemia, are associated with higher odds of severe dengue, organ dysfunction, and death.<sup>23-25</sup> The relatively higher prevalence of hyperbilirubinemia in DHF in this cohort is in keeping with recent adult and pediatric studies, where elevated total bilirubin correlated with severe dengue, coagulopathy, plasma leakage, and poor outcomes.<sup>25 27 26 10 23</sup> However, not all contemporary literature finds a simple linear relationship between degree of transaminase elevation and overall disease severity, and some reviews note that LFT derangements may be influenced by age, comorbidities, concomitant viral hepatitis, and hepatotoxic drugs.<sup>25</sup> The current findings contribute to

the expanding body of regional evidence from Pakistan and adjacent countries indicating that liver dysfunction is a key component of dengue pathogenesis and can aid in risk assessment. Studies in Islamabad and other Pakistani centers have found comparable patterns of AST predominance increase, common hepatomegaly, and substantial relationships between abnormal LFTs and DHF/DSS.<sup>24-30</sup>

## Conclusion

Derangements in liver function tests are common in dengue infection, and they are especially severe in dengue with hemorrhagic fever. AST elevation has a substantial correlation with illness severity and may be used as a measure for hepatic involvement. The majority of abnormalities are moderate and reversible, emphasizing the necessity of frequent liver function monitoring in hospitalized dengue patients for early diagnosis of severe illness and optimal therapy. Generating such locally relevant data would assist integrate routine LFT monitoring into dengue management algorithms, enhance severity assessment upon admission, and guide early escalation of care for high-risk patients in endemic, resource-constrained settings.

**Limitations:** The cross-sectional methodology and single center, non-probability sampling limit causal inference and generalizability, as observed in other recent LFT-based dengue research<sup>24 22 21</sup>. Serial measurements of liver enzymes, albumin, and coagulation indices were not evaluated, preventing the assessment of dynamic patterns that have been postulated as more powerful prognostic indicators than single time point data. The research also did not look at other crucial liver markers such alkaline phosphatase, INR, or synthetic function, which have been linked to mortality in other cohorts. Finally, relevant confounders such as dengue serotype, nutritional status, and pharmacological exposures were not investigated; nevertheless, these have been emphasized in previous studies as modifiers of dengue-associated hepatitis.

**Future Insights:** Despite these limitations, the current study confirms a similar message from recent literature: hepatic involvement is common in dengue, especially in DHF and severe variants, and AST rise is a valid, straightforward predictor of illness severity. Integrating regular liver function monitoring into dengue management algorithms at tertiary care facilities, particularly in endemic areas like Lahore, is expected to enhance early detection of high-risk patients and guide appropriate supportive measures<sup>31-36</sup>. Future prospective multicenter studies integrating serial LFTs, larger liver panels, and outcome measures such as ICU admission and death will help to refine prognostic thresholds and verify AST-based risk categorization in various South Asian populations.

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