

Prevalence of derangement of LFTs in dengue fever at tertiary care hospital: A cross-sectional study

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ABSTRACT

Objective: The involvement of liver is a common feature of dengue fever, and the liver enzymes are often raised, sometimes to a high degree. The objective of this study was to find out the prevalence and profile of liver function test abnormalities in the laboratory diagnosed patients with dengue fever.

Material and Methods: The Cross-sectional study was done at the Department of Medicine, Jinnah Postgraduate Medical Centre, Karachi, Pakistan. In a period of Six months. Laboratory confirmed dengue fever patients aged 18-60 years were selected using non-probability consecutive sampling and a total of 150 cases were taken in the study. Dengue infection was diagnosed by positive NS1 antigen and/or dengue IgM antibody test. SPSS version 26.0 was used to analyze data and p value < 0.05 was taken as significant.

Results: The mean age was 34.6 (SD: 11.2) years, and 92 (61.3%) participants were male. Overall, 128 (85.3%) patients were deranged with LFT. The most common abnormality was elevated AST in 119 (79.3%) patients followed by elevated ALT in 104 (69.3%), elevated ALP in 38 (25.3%) and hyperbilirubinemia in 24 (16.0%). The abnormalities of LFTs were significantly higher in patients who presented on days 5–7 compared with those who presented within 4 days of the illness (93.3% versus 73.8%, p=0.001).

Conclusion: Deranged liver function tests were prevalent in dengue fever and the most important biochemical abnormalities were of AST elevation and AST predominance.

Keywords: Alanine transaminase, Aspartate aminotransferases, Dengue, Hyperbilirubinemia, Liver function tests.

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INTRODUCTION

Dengue fever is a mosquito-borne viral disease which is a public health concern in tropical and subtropical areas. It manifests on a spectrum of clinical severity from a self-limited febrile illness to severe dengue with plasma leakage, bleeding, shock and multi-organ dysfunction. Liver involvement is known to be part of the dengue infection and disturbance in liver function tests is known to occur even before the onset of jaundice or liver failure. Children affected have been reported to have increased serum levels of aminotransferases, mainly aspartate aminotransferase and alanine aminotransferase, that have been correlated with the severity of the disease [1].

Pediatric evidence has shown that hepatic dysfunction can aid in predicting progression to severe dengue; higher transaminase, abnormal bilirubin and lower albumin levels were more

prevalent in the complicated cases [2]. A retrospective observational study reported a spectrum of liver damage throughout the spectrum of severity, with biochemical abnormalities possibly representing direct injury from the virus, systemic inflammatory process, or hypoxic mechanisms [3]. Frequent changes in aminotransferases and haematological parameters have been seen in cross-sectional data of hospitalized dengue patients [4]. Adverse outcomes and more severe disease were associated with deranged liver function tests in children in a similar fashion [5].

In addition to traditional liver tests, research has been conducted on biomarkers of liver involvement. Biochemical markers were identified in adult case-control data to enhance the recognition of liver injury in dengue and the aspartate aminotransferase-to-platelet ratio index was suggested as a good indicator of complicated infection [6-7]. However, a systematic review showed that liver involvement is frequent, but the rates for abnormalities and the degree of abnormality are variable depending on the age range, severity of the disease, context, and laboratory definition of abnormality [8]. Extreme hepatic reactions have also been described such as acute liver failure, but these are the rare end of the spectrum [9]. Meta-analytic findings suggested high

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mortality with dengue associated acute liver failure and hence the importance of timely detection of hepatic dysfunction [10].

Dengue is an important public health issue and outbreaks are repeatedly being reported from various areas of Pakistan. In Pakistan, there is a persistent burden of dengue infection with 48,906 confirmed cases and 183 fatalities reported during dengue outbreak 2021 [11]. While various studies in Pakistan have described the clinical and haematological manifestations of Dengue, there is little data available on the frequency and pattern of LFT abnormalities in adult Dengue patients [12-13]. Although, there is growing evidence of liver involvement in Dengue, information on the prevalence and pattern of liver function abnormalities among adult Dengue patients in Pakistan is still scarce. Thus, the present study was aimed to find the prevalence and profile of liver function test derangements in laboratory confirmed Dengue cases in a tertiary care hospital.

MATERIAL AND METHODS

This cross-sectional study was carried out in the Department of Medicine at Jinnah Postgraduate Medical Centre, Karachi, Pakistan for six months from 1st July 2025 till 30th December 2025 after receiving approval from the College of Physicians and Surgeons Pakistan and Institutional Review Board, Jinnah Postgraduate Medical Centre with approval No: F.2-81/2025-GENL/373/JPMC on 25th June 2025.

Sample size was determined using OpenEpi for estimating a population proportion. The calculated number of participants was 150. A prevalence of 40.0% dengue with warning signs (DWS) reported in a previous study [11] among dengue patients was used for sample size estimation, 95% confidence level and 5% absolute precision. So, 150 laboratory confirmed dengue fever patients were consecutively sampled. All adults, both male and female, between 18 - 60 years of age, who had laboratory confirmation of DF and had been admitted to the hospital within the first seven days of illness and who were willing to sign an informed consent form were included. Dengue infection was diagnosed by the presence of a positive dengue NS1 antigen and/or dengue IgM antibody by enzyme-linked immunosorbent assay or rapid diagnostic test. Patients with known chronic liver disease (hepatitis B, C or cirrhosis), those who were on hepatotoxic drugs, patients with the co-infection of malaria or typhoid and pregnant women were excluded.

Operationally, dengue fever was defined as an acute febrile illness with laboratory confirmation (positive dengue NS1 antigen and/or dengue IgM antibody test). Liver biochemical parameters deranged included, serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and total bilirubin. Hyperbilirubinemia was defined as the serum level of total bilirubin being > 1.2 mg/dL; AST predominance was defined as the serum level of AST being higher than its corresponding ALT level in the same patient and elevated AST and ALT were defined as AST and ALT serum levels > 40 IU/L. Any LFT derangement was defined as elevation of at least one biochemical parameter including AST, ALT, ALP or total bilirubin above the laboratory reference range. Liver enzyme derangement was divided into severity categories based on the extent of increase from the upper limit of normal (ULN). Mild derangement was considered as enzyme elevation $\leq 2 \times$ upper limit of normal (ULN), moderate derangement was considered as enzyme elevation $> 2 \times$ to $5 \times$ ULN, and severe derangement was considered as enzyme elevation $> 5 \times$ ULN. Eligible patients were enrolled consecutively, based on written informed consent. Demographic data (age, sex) and clinical data (time since onset of illness on admission) were collected by using a structured data collection proforma. At admission, blood samples were analyzed at the hospital laboratory following standard operating procedures (SOP). The serum AST, ALT, ALP and total bilirubin levels were measured, recorded and categorized based on predetermined operational definitions. Data were entered and analyzed with the help of the Statistical Package for the Social Sciences (SPSS) version 26.0. Shapiro-Wilk test was used to check the normality of quantitative variables. The age was normally distributed and was presented as mean $\pm$ SD while the duration of illness at admission was non-normally distributed and presented as median (IQR). Qualitative data such as gender, liver function test derangement were presented as frequency and percentage. Liver function test abnormalities were used as primary outcome, and were presented in terms of frequency and pattern and were summarized by descriptive statistics. Pearson's Chi-square test was used to determine the association between liver function test derangement and categorical variables such as gender (male and female), age group (18-35yrs and 36-60yrs), and duration of the illness at the time of admission (≤ 4 days and 5-7 days). Fisher's exact test was used for expected frequencies that

were too small. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

A total of 150 laboratory-confirmed dengue fever patients were included in the study. The average age of the participants was 34.6 (SD: 11.2) years. Among the participants, 92 (61.3%) were male and 58 (38.7%) were female. The median time of illness at the time of admission was 5 days (IQR 4–6 days). NS1 antigen was positive alone in 104 (69.3%) patients, dengue IgM antibody was positive alone in 32 (21.3%) patients and both NS1 antigen and dengue IgM antibody was positive in 14 (9.3%) patients (Table-I).

Out of all the patients, 128 (85.3%) patients had deranged liver function tests (LFT) while 22 (14.7%) patients had normal LFT results. The most common

biochemical derangement was raised AST (79.3%) followed by raised ALT (69.3%), raised ALP (25.3%) and hyperbilirubinemia (16.0%). One hundred and one patients (67.3%) had AST predominance. In the category of patients with LFT derangement, 55 (43.0%), 50 (39.1%) and 23 (18.0%) had mild, moderate and severe LFT derangement respectively. These severity percentages were calculated using the subgroup of patients with LFT derangement (n=128) as the denominator (Table-II).

But a statistically significant association was found between duration of illness at admission and LFT derangement. Patients who presented between days 5-7 of illness had higher frequency of LFT derangement (83 (93.3%)) compared with patients presenting within ≤4 days of illness (45 (73.8%)) (p=0.001) (Table-III).

Table-I. Demographic and clinical characteristics of study participants (n=150)

Characteristics	Value
Age, years	34.6 (SD: 11.2)
Age group, n (%)	
18–35 years	82 (54.7)
36–60 years	68 (45.3)
Gender, n (%)	
Male	92 (61.3)
Female	58 (38.7)
Duration of illness at admission, days	5 (IQR: 4–6)
Duration of illness at admission, n (%)	
≤4 days	61 (40.7)
5–7 days	89 (59.3)
Laboratory confirmation, n (%)	
NS1 antigen positive only	104 (69.3)
Dengue IgM antibody positive only	32 (21.3)
Both NS1 antigen and IgM antibody positive	14 (9.3)

SD: Standard deviation; IQR: Interquartile range; NS1: Non-structural protein 1; IgM: Immunoglobulin M

Table-II. Frequency and pattern of liver function test derangement among study participants (n=150)

Liver function test findings	n (%)
Any LFT derangement	128 (85.3)
No LFT derangement	22 (14.7)
Elevated AST (>40 IU/L)	119 (79.3)
Elevated ALT (>40 IU/L)	104 (69.3)
Elevated ALP above reference range	38 (25.3)
Hyperbilirubinemia (>1.2 mg/dL)	24 (16.0)
AST predominance	101 (67.3)
Severity of LFT derangement (n=128)	
Mild (≤2× ULN)	55 (43.0)
Moderate (>2–5× ULN)	50 (39.1)
Severe (>5× ULN)	23 (18.0)

LFT: Liver function test; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; ULN: Upper limit of normal. Patients could have more than one abnormal LFT parameter; therefore, percentages of individual abnormalities are not mutually exclusive. Severity categories of LFT derangement were calculated among patients with LFT derangement only (n=128), not the total study population (n=150).

Table-III. Association of liver function test derangement with demographic and clinical characteristics (n=150)

Variables	Total (n)	LFT deranged n (%)	LFT normal n (%)	p-value
Age group				0.168
18–35 years	82	67 (81.7)	15 (18.3)	
36–60 years	68	61 (89.7)	7 (10.3)	
Gender				0.098
Male	92	82 (89.1)	10 (10.9)	

Female	58	46 (79.3)	12 (20.7)	0.001
Duration of illness at admission				
≤4 days	61	45 (73.8)	16 (26.2)	
5–7 days	89	83 (93.3)	6 (6.7)	

Pearson's Chi-square test was applied to assess associations between LFT derangement and age group, gender, and duration of illness at admission. A two-tailed p-value <0.05 was considered statistically significant.

DISCUSSION

This current study assessed the frequency and trend of liver function test (LFT) derangements in hospitalized adult dengue fever patients with laboratory confirmed diagnosis of dengue fever. The results showed that 128 (85.3%) of the patients had one or more abnormal liver biochemical parameters. The most common abnormality was elevated aspartate aminotransferase (AST) followed by elevated alanine aminotransferase (ALT), elevated alkaline phosphatase (ALP), and hyperbilirubinemia. In patients with LFT derangement, majority of the patients had mild to moderate biochemical abnormalities while severe biochemical abnormalities were present in lesser numbers. These observations suggest that biochemical liver damage is a common feature of dengue infection, but clinically apparent liver failure is still rare.

Previous studies have shown that liver involvement is an important part of dengue infection ranging from minimal rises in liver enzyme to severe liver dysfunction in critical dengue patients. Juneja *et al* have reported that AHF due to dengue is a rare but serious complication and is commonly associated with serious systemic manifestations and needs intensive clinical management [13]. Although no clinical hepatic failure was recorded in the available case records, formal assessment of hepatic failure was not a study outcome in the current study. The variations between reported findings may be due to differences in patient population size, or in the severity of the disease.

The relative predominance of AST elevation over ALT elevation found in this study is similar to previous knowledge of liver injury related to dengue. Khattak *et al*. [14], reported that in dengue patients, there is often more elevation of AST than ALT levels which may be due to both hepatocellular damage and extrahepatic tissue damage, especially muscle damage from systemic viral infection. Likewise, laboratory findings of alteration of liver enzymes during dengue virus infection have been reported as a common biochemical feature of dengue virus infection which justifies the importance of assessment of aminotransferase during clinical evaluation of dengue patients [15].

In the present study, the duration of illness at admission was significantly associated with LFT

derangements. There was a higher proportion of LFT abnormalities among patients who presented between days 5 and 7 of illness than in patients who presented on or before day 4 of illness (93.3% vs 73.8%, $p=0.001$). Past studies have indicated that there is possibility of increasing inflammatory response, oxidative stress and systemic effects of viral infection, which may be the reason for the hepatic injury becoming more predominant during the critical phase of the disease [15]. This study was cross sectional; however, biochemical parameters were only measured at the time of admission and the time course of liver abnormalities could not be determined.

The mechanisms by which the liver is involved in dengue are thought to be multifaceted. Hepatocellular damage during infection could involve direct viral damage, immune-mediated injury, oxidative stress, and circulatory disturbances [17-18]. Other studies have investigated the potential value of liver-related indices such as MELD score, albumin-bilirubin index, and AST-to-platelet ratio index in identifying patients who are at higher risk for adverse outcomes [16]. In the present study, however, these markers of prognosis were not evaluated and the clinical applicability could not be determined.

Chronic liver disease, hepatotoxic drug use, malaria and typhoid infection were excluded to increase the probability that biochemical abnormalities observed were associated with dengue infection. But in endemic areas, other viral infections and unknown contributing factors could affect liver enzyme levels and should be considered when interpreting the findings [19]. Liver damage has also been reported in severe cases of dengue without circulatory shock, which suggests that dengue related liver damage may be multifactorial, and not only due to hypoperfusion.²⁰ A more complex intertwining of immunological and metabolic aspects of dengue infection also implies a relationship between the virus and hepatic disease, as recent evidence suggests [21].

The strengths of this study are laboratory confirmation of dengue cases, the use of multiple biochemical parameters like AST, ALT, ALP and bilirubin, the use of a predesigned operational definition of biochemical abnormalities and the evaluation of demographic and clinical associations.

These results give local data on biochemical profile of hepatic involvement in hospitalized dengue patients. To conclude, this study confirms that biochemical liver abnormality is very common in hospitalized patients with dengue fever and elevation of AST is chief biochemical abnormality. There was a significant association of LFT derangement with longer duration of illness at admission. These results highlight the need of biochemical evaluation of the liver in the management of the disease dengue, especially in the late phase of the illness. Further multicenter prospective studies that include dengue severity classification with serial LFT monitoring and outcomes are needed to better elucidate the role of liver involvement in dengue fever.

LIMITATION

There are also a number of limitations. First, it was a single-centre study in a tertiary care hospital and so the results may not apply to all patients with dengue, particularly those treated in primary and outpatient care. Second, there may be selection bias in non-probability consecutive sampling. Third, dengue severity classification was not done; it restricted the evaluation of the association of LFT abnormality to the severity of the disease. Fourth, as no serial LFT measurements were available, it was not possible to assess temporal changes in biochemical abnormalities. Lastly, major causes of hepatic injury were excluded, but there may have been residual confounding factors. Furthermore, the number of patients included in the study was constrained by the number of eligible patients at the time of the study, which may have affected the precision of the analyses for subgroups.

CONCLUSION

Abnormal liver function tests were highly prevalent among laboratory-confirmed dengue fever patients admitted to the hospital. The most common biochemical abnormality was elevated aspartate aminotransferase (AST), followed by elevated alanine aminotransferase (ALT), elevated alkaline phosphatase (ALP), and hyperbilirubinemia. Biochemical abnormalities were predominantly mild to moderate with less severe biochemical derangements. A higher frequency of liver function test derangement was seen to be significantly associated with presentation during days 5-7 of illness. This finding reveals the occurrence and the profile of biochemical abnormalities in the liver of hospitalized patients with dengue.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHORS CONTRIBUTION

Jameel Ahmed: Substantial contribution to study design, data collection, manuscript preparation, critical review, final approval, responsible for every aspect of the research

Muhammad Omer Sultan: Substantial contribution to study design, data collection, manuscript preparation, critical review, final approval, responsible for every aspect of the research

Kiran Sajjad: Substantial contribution to study design, data collection, manuscript preparation, critical review, final approval, responsible for every aspect of the research

Balram Das: Substantial contribution to study design, data collection, manuscript preparation, critical review, final approval, responsible for every aspect of the research

Muhammad Ghufraan and Abdul Sattar: Substantial contribution to study design, data collection, manuscript preparation, critical review, final approval, responsible for every aspect of the research

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