

# Assessment of Liver Function Test Abnormalities in Adult Dengue Patients at Mardan Medical Complex, Mardan

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## Abstract

**Background:** Background: Dengue virus infection is a major public health concern in tropical regions and is frequently associated with hepatic involvement. Liver dysfunction ranging from mild transaminase elevation to severe hepatic injury has been reported in dengue patients.

**Objective:** To assess the clinical significance of liver function tests abnormalities in adult patients with dengue virus infection

**Methods:** This was across-sectional study undertaken at the Department of Medicine, Mardan Medical Complex (MMC), Mardan, from January 2022 to December 2023. A total of 200 participants were included, comprising 88 laboratory confirmed dengue patients and 112 healthy controls. Dengue infection was confirmed using dengue IgM enzyme linked immunosorbent assay (ELISA). Venous blood samples were collected and analyzed for liver function parameters, including serum bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and serum albumin, using standardized automated methods. Patients with chronic liver disease, alcohol use, hepatotoxic drugs exposure, Nephrotic syndrome or other confounding conditions were excluded. Data was analyzed using SPSS version 26, applying the independent t-test, with a  $p$  value  $<0.05$ .

**Results:** Of the 88 patients examined, 62(70.45%) were male and 26 (29.54%) were females. The patients' ages ranged from 18 to 60 years, with a mean age of 37.69 years. Most of the dengue patients were males. The highest number of dengue cases were reported among those aged between 31 to 45 years. Compare control group, LFT's of the dengue patients showed significant elevation of S Bilirubin, ALT, AST and significantly lower level of S albumin ( $p <0.05$ ).

**Conclusion:** Dengue virus infection is commonly associated with hepatic dysfunction, characterized by elevated transaminases and hypoalbuminemia. AST elevation was more prominent than ALT, a characteristic biochemical feature of dengue infection. Routine assessment of liver function tests should be considered an essential component of dengue patients' evaluation, as early identification of hepatic involvement may help predict disease severity and guide clinical management of dengue patients.

**Key words:** Dengue fever, liver function tests, AST, ALT.

## Introduction

The most prevalent and acute arboviral illness, dengue is caused by a flavivirus and is spread from an infected person to a healthy person by a female mosquito called *Aedes Aegypti*. It is predominantly present in more than one hundred countries in tropical and subtropical regions and often causes epidemics and even pandemics. The WHO estimated 1.2 million infections and around 15,000 fatalities during the epidemic in 1998. The number of cases and fatalities is predicted to be 12,000 per year, with an annual increase of 50 million infections.<sup>1</sup> Dengue virus infection is a major public health problem for an estimated 3.9 billion

people, with 70% of disease burden is in Asia. All four serotypes of the dengue virus are found there,

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### Authors Contribution

MIA conceptualized the project. MAK did the data collection. SA & MKK performed the statistical analysis. MG did the literature search. Drafting, revision & writing of manuscript were done by MZ.

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namely, dengue virus 1 (DENV1), dengue virus 2 (DENV2), dengue virus 3 (DENV3) and dengue virus 4 (DENV4). Classical dengue fever frequently affects older children. Moreover, dengue may present in more severe forms, such as dengue shock or dengue hemorrhagic manifestations.<sup>2</sup> Dengue infections target the liver with involvement ranging from elevated aminotransferase enzyme to fulminant hepatic failure, which can be fatal.<sup>3</sup> Elevations in liver enzymes peak in the convalescent phase of the disease which can be deadly. Liver enzymes that are frequently seen during convalescent phase of dengue fever affecting 65 to 97 percent of patients, include aspartate aminotransferase enzymes (AST) and alanine aminotransferase enzymes (ALT).<sup>4</sup> Dengue fever triggers an inflammatory response that results in alterations to the liver parenchyma and the release of transaminases into the bloodstream.<sup>5</sup> Hepatotoxic medication usage, diabetes, hemoglobinopathies, race, and underlying liver injury are further significant variables.<sup>4</sup> Fulminant liver failure has been linked to jaundice in dengue infections.<sup>6</sup> One important plasma protein that helps to maintain plasma colloid osmotic pressure and pH is albumin.<sup>7</sup> Low blood albumin levels may be the consequence of plasma leakage in cases of severe dengue.<sup>8,9</sup> Given the high burden of dengue in endemic regions and the clinical significance of hepatic involvement, this study aimed to evaluate serum liver enzymes and albumin levels in adult patients with dengue virus infection and to compare hepatic dysfunction between dengue positive patients and healthy controls.

## Methods

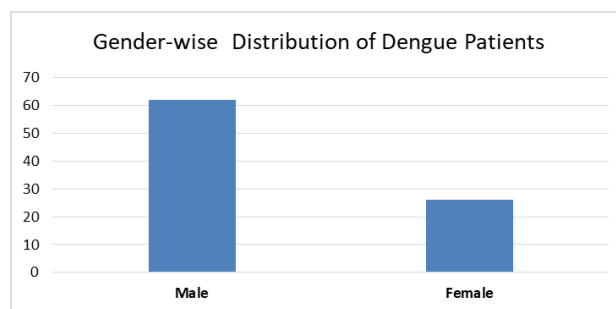
A cross sectional descriptive study was conducted at department of medicine, Mardan Medical Complex (MMC), Mardan, a tertiary care hospital, from January 2022 to December 2023. Adult patients aged 18-60 years with laboratory confirmed dengue virus infection were included. Diagnosis was established by positive NS1 antigen, dengue IGM antibodies or polymerase chain reaction. Patients aged 18-60 years of either sex who provided informed consent were enrolled. Patients having chronic liver disease, history of alcohol consumption, hepatotoxic drugs use, co-infection with typhoid or malaria or pregnancy were excluded to minimize confounding. Using the prevalence formula with an assumed prevalence of 50%, a 95% confidence interval and a 5% margin of error, a total sample size of 200 participants was obtained, comprising 88 dengue patients and 112 controls. Healthy, age and sex

matched individuals were recruited from local community as controls after written informed consent. Non-probability consecutive sampling technique was employed.

Demographic and clinical data were recorded using a structured formula. Five milliliters of venous blood were collected under aseptic conditions and serum was separated by centrifugation. Liver function tests including serum bilirubin (total and direct), ALT, AST, ALP, serum total protein, albumin and prothrombin time were analyzed using automated chemistry analyzers at MMC laboratory. Liver Dysfunction is defined as elevation of serum ALT, AST (>40 IU/L), serum bilirubin (>1.2 mg/dL), and ALP (>120 IU/L) while Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) were defined as per WHO criteria. Data were analyzed using SPSS version 26. Continuous variables were expressed as mean  $\pm$  standard deviation or median (interquartile range), while categorical variables were presented as frequencies and percentages. Group comparisons were performed using independent t-test or chi square test as appropriate. A *p*-value of <0.05 was considered statistically significant.

## Results

A total of 200 participants were included in the study, comprising 88 confirmed dengue patients and 112 healthy controls. Among the dengue patients, 26 (29.54%) were females and 62 (70.45%) were males, indicating a male predominance (Figure-1). The age of dengue patients ranged from 18 to 60 years, with a mean age of 37.69 years. The highest number of dengue cases was observed in the 31-45 years age group (Figure-2).



**Figure 1: Gender-wise distribution among study participants.**

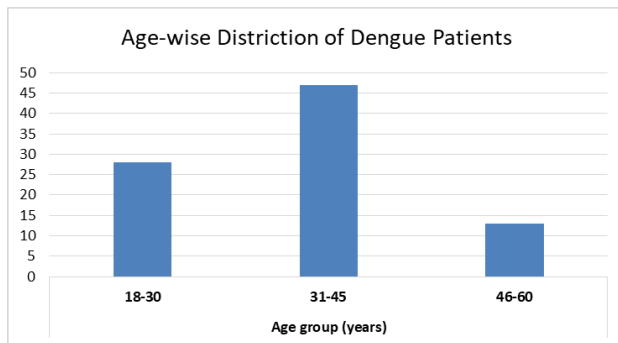
Table shows the mean ( $\pm$ SD) of serum albumin, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), and total bilirubin for both the control group and

**Table: Profile of liver enzymes in patients with dengue fever and control group.**

Parameters	Dengue patients (Mean±SD)	Controls (Mean±SD)	t-value	p Value
Total bilirubin(mg/dl)	1.21±0.14	0.801±0.08	23.788	<0.0001
Aspartate Transaminase (U/L)	362.78±37.1	38.52±4.20	81.404	<0.0001
Alanine Transaminase (U/L)	204.5±11.8	35.11±4.08	127.26	<0.0001
Alkaline Phosphatase (U/L)	131.7±3.62	109.44±9.9	19.704	<0.0001
Serumalbumin(g/dl)	3.13±0.243	4.19±0.56	16.191	<0.0001

ESS: extremely statistically significant.

dengue patients. Compared to normal persons, dengue patients had substantially higher levels of total bilirubin, AST, ALT, and ALP, and lower level of serum albumin. Eighty (90.9%) of the patients had elevated AST, while seventy-seven (87.5%) had elevated ALT. With a *p*-value of less than 0.0001, the mean AST value (362.78±37.1) was found to be considerably greater than the mean ALT value (204.5±11.8). This difference was found to be extremely statistically significant (*p* < 0.0001).



**Figure 2: Age-wise distribution among study participants.**

## Discussion

In this study out of the 88 examined patients, 70.45% were males, with a mean age of 37.69 years. Dengue prevalence predominantly involved males, especially those 31 to 45 years old which is comparable to most Asian studies in which dengue is more common in males.<sup>10,11</sup> This finding may be attributed to increased outdoor activity and occupational exposure among males, placing them at higher risk of mosquito bites in Asian countries. This is in contrast to a study conducted in south American population which showed that dengue was more common in females showing male to female ratio of 0.65-1.<sup>12</sup> In this study dengue is more common in age group 31-45 years with mean being 37.69 which is higher than that reported by Gandhi K et al in 2013 which shows that dengue is more common in age group 18-30 years with mean 34.8years.<sup>13</sup> Similarly Kumar M et al reported a higher incidence of dengue infection in individuals younger than 30 years.<sup>14</sup> Biochemical analysis

revealed markedly elevated total bilirubin, AST, ALT, and ALP levels along with diminished serum albumin compared to controls. These findings highlight the importance of LFT's in dengue patients, to differentiate it from other febrile illnesses like chikungunya.<sup>15</sup> Notably serum AST values were higher than ALT along with platelets deficiency a characteristic feature of dengue infection and Dengue hemorrhagic fever. These parameters between dengue patients and controls proved statistically significant (*p* < 0.0001).<sup>16</sup> The results of this study aligned with and added to existing knowledge regarding hepatic involvement in dengue fever and particularly the predominance of elevated S.AST over S. ALT.<sup>17</sup> In this study AST level was significantly higher than ALT (*p* < 0.0001). This pattern is characteristic of dengue infection and may reflect extra hepatic involvement, particularly skeletal and cardiac injury, as AST is present in multiple tissues. Consistent with prior Pakistani reports, a higher prevalence of dengue cases among males particularly certain age groups was found. This distribution may reflect gender-based differences in mosquito exposure or immune response within the Pakistani context.<sup>18</sup> Elevated liver enzymes level observed in this study are comparable to findings published by Pakistani researchers; specifically elevated AST and ALT in dengue patients indicated hepatic dysfunction.<sup>19</sup> Dengue induced liver inflammation causes such enzymes to be released into the bloodstream. Furthermore the significantly lower serum albumin levels in dengue patients support the previous findings from Pakistani studies suggesting plasma leakage as a consequence of severe dengue.<sup>20</sup> Decreased albumin contributes to dengue hemorrhagic fever and shock syndrome pathogenesis. Overall, the statistically significant differences in liver enzyme profile between dengue patients and controls underscore the importance of routine monitoring of LFTs for dengue cases in Pakistan. These findings are consistent with prior Pakistani studies emphasizing the role of liver function tests in assessing disease severity and guiding clinical management.<sup>21</sup> Early detection of hepatic involvement may facilitate risk stratification, timely intervention and prevention of severe complications.

## Conclusion

All types of dengue infections frequently caused liver damage with resultant increase in liver enzymes; AST rising much higher than ALT. Patients with dengue infection had considerably increased serum levels of ALT, bilirubin, and ALP. Elevated AST might function as a predictor to dengue fever. Alteration in vascular permeability can also be indicated by low serum albumin (hypoalbuminemia). Increases in ALT, bilirubin, and ALP level may be poor indicators of prognosis.

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**Availability of Data:** The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Ethical Approval:** The Institutional Review Board of Mardan Medical Complex, Mardan approved the study via letter no. 54-57/ERC 2021 MMC dated 21/12/2021.

**Conflict of Interest:** None declared.

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