

## Original Research Article

# Analysis of liver function tests in dengue fever

Denesh Narasimhan\*, Pasupathi Ponnusamy, M. Sathish

Department of Medicine, PSG Institute of Medical Sciences and Research, Peelamedu, Coimbatore, Tamil Nadu, India

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**\*Correspondence:**

Dr. Denesh Narasimhan,

E-mail: [dnarasim@yahoo.com](mailto:dnarasim@yahoo.com)

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### ABSTRACT

**Background:** Dengue fever is an exceedingly common tropical infection in India. It can affect the liver with a wide spectrum of manifestations. The aim of the study was to analyse the liver function tests derangement in serologically proven dengue cases.

**Methods:** Patients who were Dengue IgM positive were included in this study. All the patients underwent liver function tests.

**Results:** Of 100 patients, 33% had less than 2-fold increase in ALT levels, 18% had 2-4-fold increase, 20% had 4-10-fold increase and 11% had more than 10-fold increase. Overall 18% had normal values and 82% had values of ALT above normal. With regard to AST 8% had normal values, 26% had less than 2-fold normal, 26% had 2-4-fold increase, 25% had 4-10-fold increase and 15% had greater than 10-fold increase. 92% of patients had values above normal. Bilirubin levels were elevated in 5% of cases. Alkaline phosphatase levels were elevated in 25% of cases; serum globulins were increased in 9% of cases. Serum proteins were low in 43% of cases and serum albumin was low in 31% of cases.

**Conclusions:** The spectrum of hepatic involvement in dengue fever can vary from asymptomatic biochemical involvement to severe acute liver cell injury. Hyperbilirubinemia may also be observed. Low albumin levels may be present and may be a marker of the critical phase of the disease.

**Keywords:** ALT, AST, Dengue fever, Hyperbilirubinemia

### INTRODUCTION

Dengue is one of the most important mosquito borne viral diseases which is spreading rapidly throughout the world. It has increased exponentially in the last five decades. There are about 50million new dengue infections occurring each year worldwide.<sup>1</sup> There are about 2.5billion people living in areas where dengue is endemic and hence potentially at risk for infection. The number of dengue cases has gone up from 15497 cases in 1960-1969 to 925896 cases in 2000-2007.<sup>2</sup>

Multiple outbreaks of dengue have happened in India. Reports have come from Bangalore, Punjab and Delhi.<sup>3-5</sup>

Most of these cases have been reported in the post monsoon season from September to November. Dengue fever can affect multiple organ systems. There have been reports of dengue fever involving heart, nervous system and liver causing myocarditis, encephalitis and hepatitis. This present study is an analysis of liver function tests abnormalities in dengue fever.

### METHODS

Our present study is a retrospective observational analysis of 100 serologically proven dengue patients admitted at PSG Hospital from January to September 2017. Inclusion criteria included patients more than 15

years of age, dengue IgM positive. Exclusion criteria consisted of patients with pre existing liver disease, scrub typhus, malaria and typhoid. All a patient underwent liver function testing.

Bilirubin testing was done by diazo method, alanine aminotransferase [ALT] was tested by IFCC method, aspartate aminotransferase [AST] was tested by IFCC method. Alkaline phosphatase was tested by IFCC method. Serum proteins were tested by Biuret method, Serum albumin was tested by BCG, dyebind method and serum globulin levels were calculated. Dengue serology was done by ELISA method.

**RESULTS**

All patients underwent liver function tests. Of 100 patients, 33% had less than 2 fold increase in ALT levels, 18% had 2-4 fold increase, 20% had 4-10 fold increase and 11% had more than 10 fold increase.

Overall 18% had normal values and 82% had values of ALT above normal. With regard to AST 8% had normal values, 26% had less than 2 fold normal, 26% had 2-4 fold increase, 25% had 4-10 fold increase and 15% had greater than 10 fold increase. 92% of patients had values above normal.

Bilirubin levels were elevated in 5% of cases. Alkaline phosphatase levels were elevated in 25% of cases, serum globulins were increased in 9% of cases. Serum proteins were low in 43% of cases and serum albumin was low in 31% of cases.

**Table 1: Range of aminotransferase elevations in dengue fever.**

	ALT number	ALT %	AST number	AST %
Normal	18	18	8	8
<Two fold rise	33	33	26	26
Two-four fold rise	18	18	26	26
Four-ten fold rise	20	20	25	25
>Ten fold rise	11	11	15	15

**Table 2: Ranges of increased bilirubin, alkaline phosphatase and globulin levels.**

Tests	Number	%
Bilirubin > 2mg/dl	5	5
Alkaline phosphatase increased	25	25
Serum globulins increased	9	9

**Table 3: Range of protein levels in dengue fever.**

Serum proteins	Number	%
Low	43	43
Normal	57	57
Increased	0	0

**Table 4: Range of serum albumin levels in dengue fever.**

Serum albumin	Number	%
Low	31	31
Normal	69	69
Increased	0	0

**DISCUSSION**

Dengue infection is known to affect the liver. The liver injury is not fully manifest in the early stages of dengue fever. The cause for the liver dysfunction is thought to be multifactorial. It is postulated that liver damage may happen secondary to hypoxia, direct effect of virus or immune mediated damage.<sup>6</sup> The spectrum of liver involvement in dengue fever varies from asymptomatic elevation of transaminases to severe liver involvement in the form of acute liver cell failure. Dengue virus targets the hepatocytes and the kupffer cells in the liver.<sup>7</sup> Virus enters the cells by binding to receptors and is taken inside the cell by endocytosis.

The final outcome of hepatic involvement is apoptosis of cells. Biopsies done on patients with dengue fever have revealed patterns such as microvascular steatosis, liver cell necrosis, councilman bodies and portal tract inflammation.<sup>8</sup>

Asymptomatic derangement in liver function tests are common findings. Rarely dengue fever can cause acute liver cell injury. Patients may present with pain in the right hypochondrium, hepatomegaly and jaundice.<sup>9</sup>

In a study by Amit Soni et al, with regards to AST levels, it was shown that 45.6% had less than 3 fold elevation, 36.7% had 3-10 fold elevation and 16.4% had greater than 10 fold elevation.<sup>10</sup> In the same study with regards to ALT, 27.8% had 1-3 fold elevation, 59.4% had 3-10 fold elevation and 8.9% had greater than 10 fold elevation. In this study AST elevation was more than ALT which was similar to our study. The increased AST/ALT ratios can be used to differentiate dengue infection from viral hepatitis where it is infrequently seen.<sup>7</sup> The incidence of AST and ALT elevations more than 10 fold were also comparable to our study.

In a study by Parkash et al, 3.1% of patients had hyperbilirubinemia which was comparable to our study which had 5 %.<sup>11</sup> Larreal Y et al in their study had reported hyperbilirubinemia in 2 out of 63 cases.<sup>12</sup>

In a study by Samatha Fernando et al, serum proteins were low in 63.6% of cases and serum albumin was low in 54.5% of cases.<sup>6</sup> This was in slight variance with our study where serum proteins were low in 43% and serum albumin was low in 31% of cases. In a study by Brito et al, it was shown that 71% of cases with dengue hemorrhagic fever had hypoalbuminemia concluding that serum albumin level was a marker for critical stage of the

infection where there was increased vascular permeability.<sup>12</sup> Our study did not differentiate between classical dengue and dengue hemorrhagic fever.

In a study by Rajoo Singh Chhina et al, alkaline phosphatase levels were elevated in 30.3% of cases with dengue fever and 40% of cases with dengue hemorrhagic fever.<sup>13</sup> This was comparable to our study where alkaline phosphatase was elevated in 25% of cases.

## CONCLUSION

The spectrum of hepatic involvement in dengue fever can vary from asymptomatic biochemical involvement to severe acute liver cell injury. Hyperbilirubinemia may also be observed. Low albumin levels may be present and may be a marker of the critical phase of the disease. Treatment is usually supportive. Limitation of this study is that differentiation between classical dengue fever and dengue hemorrhagic fever was not done. Also, coagulation function of the liver in the form of prothrombin time was not assessed especially in patients with severe elevations of aminotransferases.

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