

SPECTRUM OF HEPATIC INVOLVEMENT IN PATIENTS WITH DENGUE INFECTION

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ABSTRACT

Background: dengue infection is a public health situation which requiring immediate action because of its capacity to metastasize exponentially beyond geographical borders. There are around more than 50 million new dengue infections encountered each year all around the globe. **Material & Methods:** The present study was a retrospective observational type study which includes 100 patients of dengue which were serologically proven and who were admitted at American international institute of medical sciences, GBH Hospital, Bedwas, Udaipur, Rajasthan. The study was conducted from May 2017 to October 2017. **Results:** Out of total 100 patients, 37 had less than 2 fold raised titer of ALT levels, 20 had 2-4 folds raised ALT levels, 21 had 4-10 folds raised ALT levels and 10 had more than 10 fold raised ALT levels. 9 had a normal titer of AST values, 25 had less than 2 fold titer normal AST values, 24 had 2-4 fold raised AST titer than normal values, 28 had 4-10 fold raised AST values and 14 had greater than 10 fold raised AST values than the normal range. Bilirubin levels were elevated in 10 patients, alkaline phosphatase levels were elevated in 29%, and serum globulins were elevated in 11 patients. Serum proteins were below the normal range in 46% and serum albumin was below normal in 35% of patients. **Conclusion:** We concluded that range of liver function deterioration in dengue fever can vary from asymptomatic to symptomatic biochemical involvement and beyond to severe acute liver cell injury. Low serum albumin levels observed which can be used as a marker of the critical phase of the liver disease.

Keywords: ALT, AST, Dengue fever, Hyperbilirubinemia

INTRODUCTION

Dengue is one of the most overriding mosquitoes borne viral disease mediate by the bite of the infected Aedes mosquito which is expanding rapidly throughout the globe. It has risen more and more rapidly in the last few decades (1). World health organization has clearly expressed that dengue infection can be contemplated to be a public health situation which requiring immediate action because of its capacity to metastasize exponentially beyond geographical borders. There are around more than 50 million new dengue infections encountered each year

all around the globe (2). There are more than 2.5 billion people inhabited in areas where dengue is prevalent and hence potentially endemic zone for infection. The prevalence of dengue cases has gone up from 15495 cases in 1960-1970 to 925900 cases in 1999-2007 (3).

Dengue infection displays greater variance in its occurrences with high epidemic and non-epidemic variability. It can manifest as vast epidemics of disease along with seasonal variation. Dengue virus has multiple serotypes which are prevalent in India.

Multiple epidemics of dengue had happened in India. Reports have come from all geographical regions of the country (4). Dengue virus-related diseases can be classified into dengue fever, undifferentiated fever and dengue hemorrhagic fever (5). Dengue hemorrhagic fever is subcategorized into four subtypes out of which third and fourth is representative of dengue shock syndrome. Most of the dengue patients have been reported in the post-rainy period from September to November (6).

There have been reports of dengue fever has the potency to affect multiple organ systems involving nervous system, heart, and liver resulting in encephalitis, myocarditis, and hepatitis. This present study was conducted to evaluate the effect of dengue on liver and abnormalities in liver function in dengue fever.

MATERIALS & METHODS

The present study was a retrospective observational type study which includes 100 patients of dengue which were serologically proven and who were admitted at American international institute of medical sciences, GBH Hospital, Bedwas, Udaipur, Rajasthan. The study was conducted from May 2017 to October 2017. Written informed consent was taken from all the patients after taking ethical approval from an ethical committee of our hospital. Inclusion criteria included patients more than 15 years of age and dengue IgM antibody positive. Patients with pre-existing liver disease or scrub typhus or malaria or typhoid were excluded from the present study. All patients underwent liver function tests. Bilirubin estimation was done by the diazo method and serum alanine aminotransferase [ALT] levels were estimated by IFCC method and serum aspartate aminotransferase [AST] levels were estimated by IFCC method. Serum Alkaline phosphatase levels were estimated by IFCC method. Serum proteins were evaluated by Biuret method and Serum albumin levels were estimated by BCG dyebind method and serum globulin levels were estimated. Dengue serology for antibody was done by ELISA method. The data were analyzed using MS Excel 2010, Epi Info v7 and SPSS v22.

RESULTS

In present study total, 100 patients were enrolled by simple random sampling method. All patients underwent for a liver function test. Out of total 100 patients, 37 patients had less than 2 fold raised titer of ALT levels, 20 patients had 2-4 folds raised ALT levels, 21 patients had 4-10 folds raised ALT levels and 10 patients had more than 10 fold raised ALT levels.

Out of total 100 patients, 20 patients had a normal titer of ALT levels and 80 patients had values of ALT above than normal. (Table 1)

Out of total 100 patients, 9 patients had normal titer of AST values, 25 patients had less than 2 fold titer normal AST values, 24 patients had 2-4 fold raised AST titer than normal values, 28 patients had 4-10 fold raised AST values and 14 patients had greater than 10 fold raised AST values than normal range. Out of total 100 patients, 91 patients had values above normal while 9 patients had below normal AST values. (Table 1)

Table No.-1: Range of aminotransferase elevations in dengue fever.

	ALT number	ALT %	AST number	AST %
Normal	20	20	9	9
<Two fold rise	27	27	25	25
Two- four fold rise	20	20	24	24
Four-ten fold rise	21	21	28	28
>Ten fold rise	10	10	14	14

Table No.-2: Ranges of increased bilirubin, alkaline phosphatase and globulin levels.

Tests	Number	%
Bilirubin > 2mg/dl	10	10
Alkaline phosphatase increased	29	29
Serum globulins increased	11	11

Out of total 100 patients, bilirubin levels were elevated in 10 patients, alkaline phosphatase levels were elevated in 29% of patients, serum globulins were elevated in 11 patients. (Table 2) Out of total serum proteins were below the normal range in 46% of patients (Table 3) and serum albumin was below normal in 35% of patients. (Table 4)

Table No.-3: Range of protein levels in dengue fever.

Serum proteins	Number	%
Low	46	46
Normal	54	54
Increased	0	0

Table No.-4: Range of serum albumin levels in dengue fever.

Serum albumin	Number	%
Low	35	35
Normal	65	65
Increased	0	0

DISCUSSION

Dengue virus infection has known the tendency to affect the liver. The liver injury is though not fully characterized in the early phases of dengue fever. The cause for the liver function deteriorations was

thought to be multifactorial etiology. It was hypothesized that liver damage may be happen secondary to hypoxic injury, the direct effect of the virus and also the immune-mediated damage (7). The spectrum of liver damage in dengue fever varies from the asymptomatic rise of serum transaminases to severe liver damage which includes incidence of acute liver cell failure. Dengue virus aims the hepatocytes and also target the kupffer cells in the liver (8). The virus infects the cells by attaching to receptors and binds than taken inside the cell by the process of endocytosis.

The conclusive prognosis of hepatic dissemination is apoptosis of liver cells. Biopsies may be considered in patients with dengue fever which can reveal histopathological patterns and markers such as councilman bodies, portal tract inflammation, microvascular steatosis and liver cell necrosis (9).

Asymptomatic disturbance in values of liver function tests are common findings. It was also known that dengue fever can rarely cause acute liver cell injury. Although some patients may present with hepatomegaly, jaundice, and pain in the right hypochondrium (10).

A study conducted by Amit Soni et al, found nearly similar results to present study, they observed that 45.6% patients had less than 3 fold elevation in AST levels, 36.7% patients had 3-10 fold elevation in AST levels and 16.4% patients had greater than 10 fold elevation in serum AST levels.10 In the same study, they also observed that 27.8% patients had 1-3 fold elevation in ALT levels, 59.4% patients had 3-10 fold elevation in ALT levels and 8.9% patients had greater than 10 fold elevation in serum ALT levels. They stated in their results that AST elevation was more significant than ALT which was also similar to the present study. The increased ratios of AST/ALT can also be used to differentiate dengue virus infection from other causes of viral hepatitis where it is generally rare and infrequently present (11). The occurrence of serum AST and serum ALT elevations more than 10 fold were also nearly similar to present study.

A study conducted by Parkash et al. found that out of total 3.1% patients had hyperbilirubinemia which was nearly similar to present study which stated hyperbilirubinemia in 9% patients (12). A study conducted by Larreal Y et al observed in their study that incidence of hyperbilirubinemia was 2 out of 63 patients (13).

A study conducted by Samatha Fernando et al, found that out of total patients serum proteins were low in 63.6% patients and serum albumin levels were low in 54.5% patients (9). These results were in contrast with a present study where serum proteins were observed low in 46% patients and serum albumin was observed low in 35% of patients. A study conducted by Brito et al, it was found that out of total 71% of patients with dengue hemorrhagic fever had shown hypoalbuminemia stating that serum albumin levels can be used as a marker for a critical stage of the dengue infection where vascular permeability was increased (14). Present study was unable to differentiate between dengue hemorrhagic fever with classical dengue fever.

A study conducted by Rajoo Singh Chhina et al, found that serum alkaline phosphatase levels were observed elevated in 30.3% of patients with dengue fever and 40% of patients with dengue hemorrhagic fever (15). These results were nearly similar to present study where serum alkaline phosphatase levels were elevated in 29% of patients.

CONCLUSION

We concluded from the present study that range of liver function deterioration in dengue fever can vary from asymptomatic to symptomatic biochemical involvement and beyond to severe acute liver cell injury. Hyperbilirubinemia was also observed. Low serum albumin levels observed which may be used as a marker of the critical phase of the liver disease. Limitation of the present study was that differentiation between dengue hemorrhagic fever and classical dengue fever was not possible with the help of present study.

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