

Original Research Article

Study of liver enzyme variation in children with dengue fever

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ABSTRACT

Background: Dengue fever continues to be one of the major public health problems in large parts of the world, with an estimated 50 million dengue infections occurring annually. Liver enzyme variation is commonly seen in patients with dengue fever. This study was undertaken to assess the pattern of liver enzyme variation in children with dengue fever and to correlate it with the severity of this disease.

Methods: Observational, descriptive hospital-based study involving 100 children who were serologically positive for dengue fever. The cases were classified as Mild, Moderate and Severe Dengue based on National Guidelines of clinical management of Dengue fever, 2015 and severity was assessed in each category. The study assessed the variability of liver enzymes in these children.

Results: Aspartate Aminotransferase (AST) was elevated in 56 cases whereas Alanine Aminotransferase (ALT) was elevated in 44 cases. The elevation in liver enzymes in mild cases was 52%, moderate cases was 75% and severe cases was 100%. In cases presenting on day 1 of fever, enzymes were elevated in 0%, on day 2 in 20%, on day 3 in 38%, on day 4 in 51%, on day 5 in 90% and on day 6 in 88%.

Conclusions: Liver Enzyme (AST and ALT) elevation in Dengue is a common feature. AST elevation was more common than ALT. Highest elevation in liver enzymes were observed on 5th and 6th day of fever. Liver enzyme elevation was more commonly seen in moderate and severe cases.

Keywords: Alanine aminotransferase, Aspartate aminotransferase, Dengue fever, Liver enzyme variation

INTRODUCTION

Dengue fever is a syndrome caused by arthropod borne viruses and is characterized by biphasic fever, myalgia, rash, leukopenia and lymphadenopathy.¹

It continues to be one of the major public health problems in large parts of the world, with an estimated 50 million dengue infections occurring annually. Dengue virus antigen has been found in a variety of tissues, predominately the liver and reticuloendothelial system. Viral replication is thought to occur primarily in the macrophages.² Even though liver is not a major target organ, several pathological findings like hepatocellular necrosis, hyperplasia of Kupffer cells, inflammatory cell

infiltration have been identified in liver biopsy specimens in patients with dengue fever.³

Liver involvement in dengue fever can vary from derangement of liver enzymes, increased bilirubin and in very rare cases, acute liver failure.

There are studies which have compared the variation in liver enzymes and severity of Dengue in children. But only few exist, which have used 2015 guidelines.

This study is conducted to compare the liver enzyme variation and the severity of the Dengue fever (according to 2015 guidelines).

METHODS

Observational, descriptive hospital-based study conducted in the Department of Pediatrics in Father Muller Medical College, Mangalore, India, from October 2017 to December 2018.

Sample size (n) obtained was 100. It was calculated based on the formula,

$$n = 4pq/d^2$$

Where,
n is sample, p is prevalence and d is allowable error
Assuming p=63.34 and taking d as 15% of p

Inclusion criteria

- Children >6 months and <15 years with signs and symptoms suggestive of Dengue fever.

Exclusion criteria

- Children <6 months and >15 years of age.
- With pre-existing liver diseases.
- Other concomitant infections affecting the liver such as malaria, typhoid, hepatitis A and B.

All children with clinical suspicion of dengue fever were screened and only those who were serologically confirmed by NS1 antigen positivity by Rapid (later confirmed by IgM capture ELISA test) were included. Dengue fever was graded according to National Guidelines of clinical management of Dengue fever, 2015.

Besides detailed history, thorough clinical examination and necessary investigations, Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) was done on day of presentation. Protocol based treatment was given. Statistical analysis was done by chi-square test and Fischer's exact test wherever necessary.

RESULTS

Table 1: Pattern of liver enzyme elevation based on category.

Classification	Total number of cases	Cases with elevated liver enzymes	%
Mild Dengue	65	34	52%
Moderate Dengue	33	25	75%
Severe Dengue	2	2	100%

During the study period, out of 100 children who were serologically positive for Dengue fever, the number of cases diagnosed as Mild Dengue were 65, Moderate Dengue were 33 and Severe Dengue were 2. Out of

which 34 cases of Mild dengue, 25 cases of Moderate Dengue, and all the cases of Severe Dengue had elevated liver enzymes (Table 1).

Total number of cases with liver enzyme variations were, ALT was elevated in 44 cases and AST was elevated in 56 cases. Thus, it was found that AST was elevated in a greater number of cases as compared to ALT (Table 2).

Table 2: Pattern of liver enzyme elevation based on the day of fever.

Day of fever	Total number of cases	Number of cases with liver enzyme variation	%
Day 1	6	0	0
Day 2	15	3	20%
Day 3	13	5	38%
Day 4	29	15	51%
Day 5	20	18	90%
Day 6	17	15	88%

DISCUSSION

Hepatic dysfunction is a well-recognized abnormality in patients with dengue fever. Hepatic dysfunction in dengue may be due to the direct impact of the virus, hypoxic damage due to impaired liver perfusion resulting from fluid leakage or as a result of host immunity. Cytokines mediated liver injury has also been proposed, as IP 10 and IL 10 were found to be associated with high liver transaminase in children with dengue fever.⁵

Uncontrolled urbanization leads to inadequate management of waste and water, providing large water sources and becomes habitats for the larvae.⁶

According to the study conducted by Fernando S et al to determine the changes in the liver enzymes over the course of acute dengue infection and also the relationship of liver enzyme and the degree of viremia.⁷ It was found that all patients with severe Dengue had some degree of liver involvement while only 15.1% of those with non-severe dengue did not have any liver involvement. Authors found out that all the cases with severe dengue in this study had liver involvement (100%). While in 60.7% of non-severe (mild and moderate) cases, enzymes were elevated.

Centrilobular liver cell necrosis is a typical feature of hypoxic hepatitis, which is the liver injury observed in situations of prolonged shock.

Although liver failure has been reported in patients with prolonged shock due to dengue, it has also occurred in the absence of shock. This pattern is observed in this study too as both the cases of severe dengue had hepatic impairment.

In another study done by Jagadish kumar K and co-workers, it was found that hepatomegaly was found in 79%, hepatic tenderness in 56%, raised AST in 93% and ALT in 78% of the individuals.⁸ Whereas in this study hepatomegaly was seen in 18% of cases, hepatic tenderness was seen in 16% of cases, AST was elevated in 56% and ALT in 44% of cases. This deviation in findings in this study in severity of cases might possibly due the fact that this study had 35% of cases who were moderate to severe while in above mentioned study had 46.1%. And majority of cases in this study presented at earlier stages of the disease.

Kuo and colleagues reported elevated levels of AST and ALT were found in 93.3% and 82.2% of cases respectively.⁹ DeSouza and colleagues observed alterations of AST and ALT levels in 63% and 45% of patients respectively.¹⁰

In another study conducted by Roy A et al, cases were grouped as dengue fever without warning signs (Group 1), dengue fever with warning signs (Group 2) and Severe Dengue (Group 3).⁴ It was observed that hepatic dysfunction was more in Group 2 and group 3. There was 84.4% and 93.75% ALT and AST in group 2 and 94.5% and 95.9% ALT and AST elevation in group 3. As in this study authors had grouped the patients according to 2015 guidelines, authors found out that, there was 23.07% and 41.7% ALT and AST in mild cases and 43.4% and 63.6% ALT and AST elevation in moderate cases. In all severe Dengue cases, both the enzymes were elevated.

CONCLUSION

Enzyme elevation in Dengue is a common feature. AST elevation was more common than ALT. Highest elevation in liver enzymes were observed on 5th and 6th day of fever. Liver enzyme elevation was more commonly seen in moderate to severe cases.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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