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EVALUATION OF LIVER ENZYMES IN CHILDREN WITH DENGUE INFECTIONS

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ABSTRACT

Background: Dengue virus (DENV), the most important arthropod- borne disease is transmitted to humans by mosquitos of the Aedes family. All four dengue virus serotypes (DENV-1, DENV-2, DENV-3 and DENV-4) can cause the disease which can present as a mild self-limiting illness, dengue fever (DF), or as the more severe forms of the disease, dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS). **Aim and Objectives:** The objectives of our study was to determine the prevalence of hepatic dysfunction in patients with dengue and to correlate between the severity of the disease with the extent of hepatic dysfunction. **Materials and Method**s: 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.**Discussion and Conclusion:** Enzyme elevation in Dengue is a common feature. AST elevation was more common than ALT. Highest elevation in liver enzymes were observed on 5^{th} and 6^{th} day of fever. Liver enzyme elevation was more commonly seen in moderate to severe cases.

Key-words: dengue infections, alanine transaminase, aspartate transaminase, arthropod borne infections and hepatic dysfunction.

INTRODUCTION:

Dengue virus (DENV), the most important arthropod- borne disease is transmitted to humans by mosquitos of the *Aedes* family [1]. All four dengue virus serotypes (DENV-1, DENV-2, DENV-3 and DENV-4) can cause the disease which can present as a mild self-limiting illness,

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dengue fever (DF), or as the more severe forms of the disease, dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) [2].

The modified categorization of WHO in 2009 includes dengue with or without warning signs or severe dengue [3]. In spite of the recent categorization, the majority of the studies widely use the more popular DF, DHF and DSS classification for case definition. Dengue virus infection is a public health problem in tropical and subtropical regions of the world. In India, dengue is endemic in almost all States and is the leading cause of hospitalization [4].

The disease had a predominant urban distribution a few decades earlier but is now also reported from peri-urban as well as rural areas [5,6]. During 2019, the National Vector Borne Disease Control Program reported more than 1.5 lakh laboratory confirmed cases of dengue [7]. It is therefore possible that dengue disease burden is grossly under-estimated in India. Hepatic injury with dengue infection has been described since 1967 [8]. Liver dysfunction varies from mild injury with elevation of transaminases to severe hepatocyte injury, resulting in jaundice. Direct hepatotoxicity as well as deranged host immune response against the virus is responsible for the hepatic dysfunction. Though there have been isolated cases of fulminant hepatic failure, the derangements in the transaminases are usually self-limiting and may serve as a predictor for assessing the disease severity [9,10]. Limited studies are available in our geographic location to understand the pattern of liver involvement in dengue patients based on 2009 WHO categorization. We have sought to address this gap in the literature by conducting a study in coastal Indian population. Our aim of the study was to assess the prevalence of hepatic dysfunction in patients with dengue and to correlate between the severity of the disease with the extent of hepatic dysfunction.

AIM AND OBJECTIVES: The objectives of our study was to determine the prevalence of hepatic dysfunction in patients with dengue and to correlate between the severity of the disease with the extent of hepatic dysfunction.

MATERIALS AND METHODS:

Study design: The retrospective cross-sectional study was conducted at our hospital in the department of paediatrics from January 2022 to December 2022.

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Sample size: We included a total of 100 children with confirmed dengue infections. (n= $4pq/d^2$)

Inclusion criteria: we included the children with confirmed dengue infections aged >6 months and <15 years both male and females after taking voluntary consent.

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.

Methodology: 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: We included a total of 100 children with confirmed dengue infections.

Table 1: Shows the pattern of liver enzymes based on category

Classification	Total number of cases	Cases with elevated liver enzymes	Percentage
Mild Dengue	60	34	56%
Moderate Dengue	36	30	83%
Severe Dengue	4	4	100%

Table 2: Shows the pattern of liver enzymes based on the day of fever

Day of fever	Total number of cases	Cases with elevated liver enzymes	Percentage
Day 1	8	0	0
Day 2	20	3	15%
Day 3	16	4	25%
Day 4	28	8	28.57%
Day 5	16	6	37.5%
Day 6	12	10	83.3%

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

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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. Uncontrolled urbanization leads to inadequate management of waste and water, providing large water sources and becomes habitats for the larvae. In the present study, we found that 56% had elevated liver enzymes in mild dengue category, 83% had elevated liver enzymes in moderate dengue category and all patients had elevated liver enzymes in severe dengue category. On the day 1 of fever none of the patients had elevated liver enzymes, one the day 2 20% had elevated enzymes, on the day 3, 25%, on the day 4 28.57%, on the day 5 37.5% and on the day 6 83.3% had elevated enzymes.

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. 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. 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. De Souza and colleagues observed alterations of AST and ALT levels in 63% and 45% of patients respectively. 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).4It was observed that hepatic dysfunction

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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.

CONCLUSION:

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

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