International Journal of Contemporary Pediatrics
Tirumani HB et al. Int J Contemp Pediatr. 2017 Nov;4(6):2012-2014
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20174650

Original Research Article

Study of hepatic involvement in children with dengue infection

Hima Bindu Tirumani*, Vinay Kumar Bejugam, Altaf Naseem, Arshad Hussain, Nizarlalani

Department of Pediatrics, Deccan College of Medical sciences, Hyderabad, Telangana, India

Received: 01 March 2017
Accepted: 28 April 2017

***Correspondence:**
Dr. Hima Bindu Tirumani,
E-mail: drhimabindu.t@gmail.com

ABSTRACT

Background: Liver dysfunction in children is variable and depends on disease severity. This study was undertaken to identify the range of hepatic involvement in children with dengue infection.
Methods: It is a cross sectional observational study conducted in serologically positive dengue fever in children aged between 1-14 years. Hepatic function was studied in all suspected cases over a period of 1 year from June 2015 to June 2016.
Results: Out of 55 cases admitted, liver function tests showed AST levels elevated more than 45U/L in 20 (86.9%) DF, 29 (100%) DHF, 3 (100%) DSS patients. ALT levels were elevated more than 45U/L in 16 (69.5%) DF, 24 (82.75%) DHF, 3 (100%) DSS patients. More than 10 fold increase in levels of both AST and ALT was seen in severe dengue.
Conclusions: Dengue infection is associated with variable levels of liver dysfunction. The incidence of hepatic dysfunction is more in patients with dengue fever with warning signs and severe dengue. Significant elevation of transaminase levels helps in predicting the occurrence of severe dengue. It is important to be aware of this entity which needs significant attention and management.

Keywords: AST, ALT, Liver dysfunction, Transaminases

INTRODUCTION

Dengue is a self-limiting acute mosquito transmitted disease caused by an arbovirus and spread by aedes mosquitoes. Dengue is one of the most important emerging viral disease of humans in the world afflicting humanity in terms of morbidity and mortality. Currently the disease is endemic in all continents except Europe. Dengue viruses cause symptomatic systemic and dynamic disease or asymptomatic seroconversion. It has a wide clinical spectrum that includes both severe and non-severe clinical manifestations.[1] After the incubation period, the illness begins abruptly and in patients with moderate to severe disease is followed by febrile, critical and recovery phases.

It can be difficult to distinguish dengue clinically from non-dengue febrile diseases in the early febrile phase. The liver may be enlarged and tender after a few days of fever.[2] Fever, malaise, vomiting, liver enlargement and elevated liver enzymes may be misdiagnosed as infective hepatitis and vice versa.[3] Although dengue virus is a non hepatotropic virus features of liver dysfunction can be seen in dengue.

Acute liver or renal failure and encephalopathy may be present in severe dengue.[4-9] These have been described even in the absence of severe plasma leakage or shock.[4-9] The severity of disease will usually be apparent around defervescence which coincides with the onset of the critical phase.

The aim of this study is to provide information on the hepatic involvement in children with dengue infection and highlight the importance of early recognition of severe forms of dengue infection.

METHODS

This cross sectional observational study was conducted over a period of one year in a tertiary level hospital in Hyderabad, Telangana. 55 children aged 1year to 14 years were included in the study during June 2015 to June 2016.The data was collected prospectively. The diagnosis of dengue infection was based on clinical features like fever of 1 to 5 days duration, body aches, headache, arthralgia, vomitings, skin rash, petechiae, mucosal bleeds, hepatomegaly, jaundice, abdominal pain and serologically confirmed by NS1 antigen or IgM ELISA. Children with pre-existing liver diseases, other concomitant infections affecting the liver such as malaria, enteric fever, hepatitis A, hepatitis B were excluded by history, examination and investigations. All cases were subjected to appropriate investigations like complete blood picture, liver function tests, ultrasonography of the thorax and abdomen. The study group was divided into dengue fever without warning signs (DF), dengue fever with warning signs or dengue haemorrhagic fever (DHF) and severe dengue or dengue shock syndrome (DSS) according to revised WHO 2009 criteria. Standard statistical method was used to define the measure of outcome.

RESULTS

During the one year study period in the tertiary level care hospital, 55 children were admitted with serologically confirmed dengue. Out of these 28 (51%) cases were females and 27 (49%) cases were male children. All patients were serologically positive for dengue infection.

Table 1: Clinical manifestations of dengue infection.

Clinical features	Number	%
Fever of 1 to 5 days duration	55	100
Body aches	46	83
Vomitings	55	100
Sore throat, conjunctival congestion	16	29
Petechiae, mucosal bleeds	12	21
Abdominal Pain	15	27
Hepatomegaly	5	9

NS1 was positive in 24 (43%) of children and IgM was positive in 31 (56%) of children. The study group included 23 (41.8%) of patients as dengue fever without warning signs, 29 (52.7%) as dengue fever with warning signs (dengue haemorrhagic fever) and 3 (5.5%) cases as severe dengue (dengue shock syndrome).

All (100%) the patients presented with fever of 1 to 5 days duration. Fever was associated with body aches, headache and arthralgia in 46 (83%) of children, anorexia, nausea and vomiting was found in all (100%) cases.16 (29%) had sore throat, injected pharynx and conjunctival congestion, 12 (21%) cases presented with petechiae and mucosal bleeding. Abdominal pain was present in 15 (27%) cases out of which 5 (9%) had liver enlargement more than 2 cm.

Table 2: Distribution of dengue cases.

Dengue cases	Number	%
Dengue fever	23	41.8
Dengue with warning signs (DHF)	29	52.7
Severe dengue (DSS)	3	5.45

Liver function tests showed AST levels elevated more than 45U/L in 20 (86.9%) DF, 29 (100%) DHF, 3 (100%) DSS patients. ALT levels were elevated more than 45U/L in 16 (69.5%) DF, 24 (82.75%) DHF, 3 (100%) DSS patients. More than 10 fold increase in levels of both AST and ALT was seen in severe dengue. Total protein levels less than 6g/dl was seen in 8 (14.5%) cases. Serum bilirubin levels were more than 1.5mg/dl in 3 (5%) cases with severe dengue. Ultrasound evidence of bilateral pleural effusion and ascites was noted in 28 (51%) of cases.

Table 3: Liver function of dengue patients.

	AST		ALT	
	Number	%	Number	%
Dengue fever	20	86.9	16	69.5
DHF	29	100	24	82.75
DSS	3	100	3	100

DISCUSSION

The degree of liver dysfunction in children with dengue infection varies from mild injury with elevation of transaminases to severe injury with jaundice and liver cell failure. Liver involvement may be characterised by manifestations such as pain in the right hypochondrium, hepatomegaly, varying degrees of jaundice and an increase in liver markers principally AST and ALT. The incidence of hepatic dysfunction is more in dengue shock syndrome and dengue haemorrhagic fever. Upon injury to the liver, the enzymes, aspartate aminotransferase (AST) and alanine aminotransferase (ALT), are released into the bloodstream, and as a consequence these enzymes are believed to be sensitive indicators of liver damage. In the present study the liver enzymes were elevated significantly in DHF and DSS as has been shown in numerous studies.[10-19] In the present study there was more than 10 fold increase in the levels of both AST and ALT in severe dengue. Other researchers have also observed similar results in dengue infection.[11,13]

Kuo and colleagues reported elevated levels of AST and ALT were found in 93.3% and 82.2% of cases respectively.[17] While the majority of patients had only mildly or moderately elevated levels of these transaminases, some 10% (11% and 7% for AST and ALT respectively) of patients had levels elevated by 10-fold or greater. DeSouza and colleagues observed alterations of AST and ALT levels in 63% and 45% of

patients respectively.[19] They noted that the average levels of AST and ALT were significantly higher in DHF patients than in DF patients, an observation supported by other studies. Several authors have noted that the levels of serum AST are greater than serum ALT, which is in contrast to the normal finding with viral hepatitis.[15,17,18]

Mohan B et al also reported that all cases with DHF and DSS had raised AST and ALT and the mean levels of these enzymes was significantly higher as compared to DF.[11] Roy A and Sarkar D also observed 84.4% and 93.75% ALT and AST elevation respectively in DHF and 94.5% and 95.9% ALT and AST elevation respectively in DSS.[21] Jagadish Kumar et al observed elevated ALT in 69.4% DF, 84.6% in DHF and 92% DSS and raised AST in 88% of DF,100% DHF and 96% of DSS group similar to other studies.[22]

CONCLUSION

Dengue fever has a wide clinical spectrum that includes both severe and non severe clinical manifestations. As long as DHF and DSS are recognised early and correct and timely interventions are instituted management is relatively simple, inexpensive and very effective in saving lives.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Tirumani HB, Bejugam VK, Naseem A, Hussain A, Nizarlalani. Study of hepatic involvement in children with dengue infection. Int J Contemp Pediatr 2017;4:2012-4.