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Original Research Article

Hepatic Involvement in Dengue Infected Children at Tertiary Care Hospital, Karimnagar

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ABSTRACT

Background: The spectrum of liver dysfunction in children with dengue infection is wide and is associated with severity of the disease. Dengue infection commonly causes hepatic dysfunction. The degree of liver dysfunction in children varies from mild injury with elevated transaminases to severe injury with jaundice.
Aims: To assess the spectrum of hepatic involvement in children with dengue infection.
Materials and Methods: This study was undertaken to assess the clinical and biochemical profile of hepatic involvement in children infected by dengue virus.
Results: All the cases were grouped into 3 groups, DF without warning signs, DF with warning signs and severe dengue according to revised WHO 2009 criteria. The spectrum of hepatic manifestations includes hepatomegaly, hepatic tenderness, jaundice, raised aspartate transaminase (AST), alanine transaminase (ALT) and reduced serum albumin.
Conclusions: Hepatic dysfunction was observed more in DF with warning signs and severe dengue compared to dengue without warning signs. There was elevation of ALT and AST in case of DF with warning signs and severe dengue. Therefore in a child with fever, jaundice, hepatomegaly and altered liver function tests, the diagnosis of dengue infection should be strongly considered in areas where dengue infection is endemic.

Keywords: Dengue virus, Liver function tests, Severe Dengue.

INTRODUCTION

Dengue infection is the most rapidly spreading mosquito-borne viral disease in the world with a 30 fold increase in global incidence over the last five decades and it continues to be a major challenge to public health. [1] It is estimated that about 50–100 million new dengue infections occur annually with 20,000 deaths in more than 100 endemic countries, with a steady increase in the number of countries reporting the disease. [1] Case fatality rates for the South-East Asian region are 1%, but in India, Indonesia and Myanmar, focal outbreaks have reported rates of 3%-5%. [1]

Dengue virus, a single stranded RNA virus, is categorized under the genus Flavivirus and is transmitted from an infected person to others by the bite of the female Aedes mosquito.

Hepatic dysfunction is common in dengue infection. Along with a rise in serum aminotransferases, hepatomegaly is also commonly seen in dengue infection. The spectrum of liver dysfunction in children with dengue infection is wide and it is associated with severity of the disease. The

degree of liver dysfunction in children varies from mild injury with elevated transaminases to severe injury with jaundice. [2,3] Hepatic dysfunction in dengue infection may be attributed to direct viral effect on liver cells or as a consequence of dysregulated host immune responses against the virus. [2] Jaundice in dengue infection may be associated with fulminant hepaic failure, which is a poor prognostic factor. [4]

This study was conducted to assess the spectrum of liver functions in children with dengue fever admitted in department of pediatrics of a teriiary care hospital in karimnagar.

MATERIALS AND METHODS

This study is a prospective hospital based study conducted at Chalmeda Anand Rao Institute of medical sciences, Karimnagar, Telangana, South India between March 2015 to August 2016. Ethical Committee clearance was taken from the institution and informed consent was taken from the guardian of every patient who took part in this study.

All children suspected to have dengue infection as per the revised World Health Organization (WHO) guidelines 2009, between age of 2 months and 14 years were screened. Inclusion criteria were children who were dengue Ns1Ag and IgM positive between 2 months to 14 years admitted in Chalmeda institute of medical sciences. Infants less than 2 months, Children more than 14 years, Outpatients who were not admitted in the hospital, Children with preexisting liver diseases, other concomitant infections affecting the liver such as malaria, typhoid, hepatitis A and B were excluded from the study.

A detailed history was taken and thorough clinical examination was performed in all cases and the data was collected in a predesigned proforma. All cases were subjected to the following investigations: hemoglobin, total leukocye count, differential leukocyte count, platelet count, hematocrit, peripheral blood smear, serum bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), serum albumin, serum globulin, total proteins, ultrasound abdomen.

Sample size of this study is 134 patients and 20 patients were excluded as they met the exclusion criteria. As per WHO 2009 guidelines, Dengue is classified as Dengue without warning signs, Dengue with warning signs and Severe Dengue. Probable dengue was defined as live in/travel to dengue endemic area with two of the following: Nausea, vomiting; rash; aches and pains; tourniquet test positive; leucopenia; any warning sign[1]. Warning signs include Abdominal pain or tenderness, Persistent vomiting, Clinical fluid accumulation, Mucosal bleed, Lethargy, restlessness, Liver enlargment >2 cm and increase in hematocrit concurrent with rapid decrease in platelet count[1]. Criteria for severe dengue include: Severe plasma leakage leading to: Shock (DSS), Fluid accumulation with respiratory distress; severe bleeding; Severe organ involvement- Liver: AST or ALT >=1000, CNS: Impaired consciousness, Heart and other organs.

The study population was subcategorized into dengue without warning signs (n =56) (Group 1); dengue with warning signs (n = 50) (Group 2) and severe dengue (n = 28) (Group 3) according to the WHO criteria. Statistical analysis was carried out with Microsoft Excel

RESULTS

A total of 134 children of age between 2 months and 14 were included in the study, satisfying the revised WHO 2009 criteria for DF after excluding malaria, enteric fever, hepatitis A and hepatitis B. Out of 134 children 60(44.7%) were females and 74(55.3%) were males. Minimum age of patient was 6 months and maximum age was 14 years with mean age of 8.8 years. Epidemiological and clinical features of study groups are shown in table 1.

Table 1: Epidemiological and clinical features of study groups

Parameters	Dengue without warning signs (n=56) (%) (Group 1)	Dengue with warning signs (n=50) (%)(Group 2)	Severe Dengue (n=28) (%)(Group 3)
Age(Years)	8.4	9.3	8.7
Sex(Male: Female)	34:22	28:22	12:16
Symptoms:			
Fever	56(100)	50(100)	28(100)
Bodyache	32(57.1)	44(88)	24(85.7)
Vomiting	26(46.4)	42(84)	26(92.8)
Abdominal Pain	2(3.5)	24(48)	22(79.2)
Rashes	4(7.1)	6(12)	4(14.2)
Petechiae	0	10(20)	10(35.7)
Mucosal Bleeds	0	4(8)	4(14.2)
Clinical parameters:			
Jaundice	0	6(12)	4(14.2)
Hepatomegaly	16(28.5)	28(56)	24(85.7)
Ascites	0	2(4)	22(79.2)
Bleeding manifestations	0	32(64)	20(71.4)
Shock	0	0	12(42.8)

All patients suffered from fever (100%), body aches was present in 74.6% patients. Majority patients presented with fever of short duration, but 22 (16.4%) patients had prolonged history of fever >10 days. Abdominal pain was present in 3.5%, 48% and 79.2% in Group 1, Group 2 and Group 3 patients respectively. Vomiting was also more in severe dengue (Group 3) in comparison with Groups 1 and 2. Maculopapular rash and petechial spots were seen in group 2 and 3. Mucosal bleeding was present in 14.2% of Group 3 patients and 8% of Group 2 patients.

Out of 134 patients, 14.2% of severe dengue (Group 3) and 12% of Dengue with warning signs group (group 2) clinically had icterus. Hepatomegaly was present in 85.7% of Group 3 and 56% of Group 2 and 28% in Group 1.

The mean hb was 12.2 mg/dl. Thrombocytopenia was present in all the cases with a minimum count of 10,000/cumm and a maximum of 1,32,000/cumm. Abnormal liver functions were significantly more in Groups 2 and 3. Table 2 shows the comparison of Lab Parameters between the groups. Mean ALT elevation was significantly more in Groups 2 and 3. Mean AST, ALP elevations were also significant in Groups 2 and 3. More than 10 fold increase in the levels of both ALT were observed mainly in Groups 2 (10) and 3 (35.5%). There was no significant difference in the liver function tests in children with or without hepatomegaly. Among those with hepatomegaly also there was no significant difference in the LFT's with/without hepatic tenderness. Ultra sound revealed gall bladder thickening more in the Group 3 (85.7%) and Group 2 (64%) compared with Group 1 (10.7%).

Table 2: Comparison of Lab Parameters

Lab parameters:	Dengue without warning signs (n=56) (%)	Dengue with warning signs (n=50) (%)	Severe Dengue (n=28) (%)
Mean platelet count	78,846	44,000	32,071
Mean Hb	12	12.7	11.9
Mean serum bilirubin	0.58	0.74	0.95
Elevated ALT	22(39.2)	24(48)	24(85.7)
Mean ALT	50.89	97.92	188.14
Elevated AST	46(82.1)	42(84)	26(92.8)
Mean AST	78.46	136	243.57
Elevated ALP	10(17.8)	44(88)	24(85.7)
Mean ALP	172.46	182.08	181.85
Mean serum albumin	3.83	3.78	3.57
Mean serum globulin	2.75	2.88	2.63
Gall bladder wall thickening (%)	6(10.7)	32(64)	24(85.7)

Of the patients with dengue without warning signs and Dengue with warning signs, 100% were cured and 26 patients (92.8%) were cured in the severe dengue group. Mortality amounted to 2 patients (7.1%) in severe dengue group due to Disseminated intravascular coagulation because of severe GI bleeding.

DISCUSSION

Liver involvement in dengue is usually manifested by hepatomegaly (clinically) or increase in liver enzymes (biochemically). [5,6] Presentation with jaundice can simulate acute hepatitis. Severe dengue can manifest with fulminant hepatic failure and has been the cause of death in many children with dengue infection. [5,6]

Out of 134 cases in our study, 60(50.7%) patients had hepatomegaly, which was more common in severe dengue (85.7%) and dengue with warning signs (84.4%). Similar association of hepatomegaly in dengue cases has been reported in 43 - 100% of cases in children. [3,4,7,8]

Jaundice was seen in only 10 children (7.4%). Jaundice was reported in 2-25% of cases by several authors. [4,9] Nimmannitya et al. reported jaundice and encephalopathy in 18 cases of dengue hemorrhagic fever of whom 10 died. [8]

Minor manifestations such as fever (100%), abdominal pain (79.2%) and vomiting (79.2%) were all more common in severe dengue. Abdominal pain (especially hepatic tenderness) was the dominant finding in 48 (35.8%) of the children, which is more prominent in children with severe dengue (79.2%). This is similar to the observations in a study from Thailand. [10] Persistent vomiting was present in 94 children (70.1%) and common (92.8%) in the severe dengue group. Bleeding manifestations were common in the severe dengue group (71.4%).

The hepatic enzymes were elevated significantly in dengue with warning signs and severe dengue groups, especially 10 fold rise when compared with dengue without warning signs group, which is similar to other studies.

Abnormal hepatic enzymes in dengue infection varies from 36.4% to 96% in various studies. [11,12] In a large study from Brazil, out of 1585 dengue cases, elevation in AST and ALT were seen in 63.4% and 45% of patients respectively, with 3.8% of cases having 10 fold increase in transaminase levels. [9,12] In our study, more than 10 fold rise in the levels of ALT and AST were observed mainly in dengue with warning signs(10%) and severe dengue(35.5%) groups.

Elevation of AST was more compared with ALT in the present study similar to other observations may be due to involvement of myocytes. [4,13] This differs from the pattern seen in viral hepatitis, in which ALT levels are usually higher than or equal to AST levels. [13]

Mechanisms of liver injury in dengue may be due to the direct effects of the virus or host immune response on liver cells, circulatory compromise, metabolic acidosis and/or hypoxia caused by hypotension or localized vascular leakage inside the liver. [14] Elevated transaminase levels have been suggested as a potential marker to help differentiate dengue from other viral infections during the early febrile phase. [9]

Other warning signs like fluid accumulation were evident in 24 children (17.9%) with 22 of them with severe dengue infection and thrombocytopenia was present in all cases (100%) with a minimum count of 10,000/cumm and a maximum of 1,32,000/cumm. Hepatic encephalopathy was seen in 2 children while Shock was seen in 15 children.

Of the patients with dengue without warning signs and Dengue with warning signs, 100% were cured and 26 patients (92.8%) were cured in the severe dengue group.

Mortality amounted to 2 patients (7.1%) in severe dengue group. Mortality from dengue appears to be important, which can only be minimized by increasing the

awareness about specific signs and symptoms of dengue, like bleeding, rash and even shock. Mass media like television plays a very important role for increasing the awareness about dengue among people.

The limitation of our study was that PT and APTT was not performed in all children and also liver biopsy was not performed for confirmation of diagnosis.

CONCLUSION

Hepatic involvement in dengue may vary from jaundice to more than 10 fold elevation of liver transaminases. Hepatomegaly is an important clinical sign. Alteration of liver function tests can occur with or without hepatomegaly. Significant rise of liver enzymes generally signifies severe dengue infection. Dengue hepatitis must be considered in addition to malaria, enteric fever and viral hepatitis, in the presence of fever, jaundice and hepatomegaly in endemic areas.

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