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RESEARCH ARTICLE

STUDY OF LIVER PROFILE IN DENGUE FEVER

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ABSTRACT:

Introduction: Dengue infection is a major health problem worldwide including our country. Dengue is an acute viral infection with potential fatal complications caused by Dengue viruses (DV) belong to family *Flaviviridae*. To evaluate the spectrum of hepatic involvement in dengue infection. Methods: 240 Children with serologically positive dengue fever aged between 1 year to 18 years screened and included in the study after excluding Malaria, enteric fever, Hepatitis A and Hepatitis B. Results: 240 children grouped into Dengue Fever (DF) (54.1%), Dengue fever with warning signs (23.3%) and severe dengue (22.5%) according to WHO criteria. The majority (76 %) were above 5 years. Fever (100%) was the chief complaint in all cases followed by myalgia (67%), pain abdomen (57%), vomiting (40%) and rashes (36%), petechiae were seen in 23% of cases. Eighteen (7.6%) children presented with jaundice. Out of 240 children abnormal liver function tests were observed in dengue fever with warning signs and severe dengue. Severity of hepatic dysfunction noticed more in severe dengue cases. More than 10 fold increase in the levels of both ALT and AST were observed. Conclusion: In dengue varying degree of liver dysfunction is observed, sever dysfunction is more associated with severe dengue. Significant rise of liver enzymes helps in recognition of severe forms of dengue infection. Presence of fever, jaundice and hepatomegaly in endemic areas should arouse the suspicion of dengue hepatitis.

Keyword: Dengue, Liver

INTRODUCTION:

Dengue infection is a major health problem worldwide including our country. Dengue is an acute viral infection with potential fatal complications. In 1780s there was an epidemic in Philadelphia with characteristic features of myalgia and arthralgia thus coined the term ‘’ break bone fever’’. Dengue viruses (DV) belong to family *Flaviviridae* and there are four serotypes of the virus referred to as DV-1, DV-2, DV-3 and DV-4. DV is a positive-stranded encapsulated RNA virus. . It is transmitted mainly by *Aedes aegypti* mosquito and also by Ae. *albopictus*. All four serotypes can cause the full spectrum of disease from a subclinical infection to a mild self-limiting disease.[1, 2,3]

CRITERIA FOR DENGUE ± WARNING SIGNS

A) PROBABLE DENGUE
Live in /travel to dengue endemic area.
Fever and 2 of the following criteria:
• Nausea, vomiting• Rash• Aches and pains• Tourniquet test positive
• Leukopenia• any warning sign

Laboratory-confirmed dengue

B) DENGUE FEVER WITH WARNING SIGNS

• Abdominal pain or tenderness• Persistent vomiting • Clinical fluid accumulation.
• Mucosal bleed• Lethargy, restlessness• Liver enlargement >2 cm.
• Laboratory: increase in HCT concurrent with rapid decrease in platelet count[4].

C) SEVERE DENGUE

i) Severe plasma leakage leading to-:
• Shock (DSS)
• Fluid accumulation with respiratory distress
ii) Severe bleedings evaluated by clinician
iii) Severe organ involvement
• Liver: AST or ALT >=1000
•CNS: Impaired consciousness• Heart and other organs[4]

UNUSUAL MANIFESTATIONS OF DENGUE

CNS

Few patients may develop coma. Encephalopathy and Encephalitis can occur. Hemorrhagic encephalopathy in DSS caused by type 3 Dengue viruses. [5,6]

GASTROINTESTINAL (GIT) AND LIVER

Hepatitis/fulminant hepatic failure, acalculous cholecystitis, acute pancreatitis, Hyperplasia of Peyer's patches, acute parotitis are some of the manifestations .Dengue fever may present with lower GI bleeding and colonoscopic features of Acute inflammatory colitis, acute liver failure which may completely recovers with supportive management, acute abdominal pain, diarrhoea, obstructive jaundice, Reye's syndrome. [6,7]

Liver involvement is in the form of hepatitis secondary to either direct viral invasion or due to consequence of inflammatory reaction. Patient may develop jaundice, with elevation of liver enzymes. Few cases may progress to fulminant hepatic failure and lead to hepatic encephalopathy. Typical features of fever, upper quadrant abdominal pain, abnormality of liver function tests, thickened GB wall without stones and positive Murphy's sign and sonographic evidence can establish a diagnosis of acute acalculus cholecystitis.[8]Acalculus cholecystitis may be seen in patients with DHF.

RESPIRATORY SYSTEM:

The increased permeability of alveolar capillary membrane may result in edema in alveoli and interstitial spaces and pulmonary haemorrhage which leads to a deterioration in pulmonary function.[5]Dengue shock syndrome is reported to be third leading causes of ARDS in pediatric intensive care setting in endemic area.

OCULAR MANIFESTATIONS:

The ophthalmologic findings mainly included retinal haemorrhage as a sign of increased vascular permeability and breakdown of inner blood retinal barrier and cotton wool spots representing micro infarction of nerve fibre layer due to occlusions of pre capillary arterioles.[9]

MATERIALS AND METHODS

This prospective study was conducted in the department of paediatrics, in Rajarajeswari Medical College and Hospital, Bangalore, from 1st January 2015 to 30th June 2015. All cases were enrolled who had clinical suspicion dengue infections per the WHO guidelines between 1 year to 18 years of age were screened and only serologically confirmed cases by dengue IgM, NS1Ag and IgG were included in the study. Informed consent was taken and cases were enrolled. Ethical committee clearance obtained from Ethical Committee of the Rajarajeswari Medical College and Hospital. A detailed history and a thorough clinical examination were done in all the cases. Data was collected in a prewritten proforma. Other diseases like Malaria, enteric fever, Hepatitis A and Hepatitis B were excluded by history, examination and investigations.

All the patients were subjected to following.

Investigations:

- Dengue card test
- complete hemogram- includes haemoglobin, total count, hematocrit, platelet count, differential count
- liver function test includes SerumBilirubin, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (AP),serum albumin, serum globulin, total proteins,
- Prothrombin time (PT) Activated partial thromboplastintime (APTT),
- peripheral smear for malaria parasite, chest x-ray, Widaltest, IgM Anti Hepatitis A virus, HbSAg,
- Ultrasound abdomen and thorax.

Statistical methods employed for data analysis are Descriptive statistics, Chi-Square test for categorical outcomes and t-test for comparison of means. A total of 245 cases formed the study group out of which 5 were excluded because of associated other infections (Hepatitis A=5).

RESULTS

The study group included 240 children aged between 1 year – 18 years satisfying the WHO criteria for dengue fever after excluding malaria, enteric fever, Hepatitis A and Hepatitis B. All 240 children were grouped into Dengue Fever (DF) (54.1%), Dengue fever with warning signs (23.3%) and severe dengue (22.5%) according to WHO criteria. The majority (76 %) were above 5 years. Fever (100%) was the chief complaint in all cases followed by myalgia(67%),pain abdomen (57%), vomiting (40%) and rashes (36%), petechiae were seen in 23% of cases. Eighteen (7.6%) children presented with jaundice as shown in table 2. Out of 240 children abnormal liver function tests were observed in dengue fever with warning signs and severe dengue. Severity of hepatic dysfunction noticed more in severe dengue cases. More than 10 fold increase in the levels of both ALT and AST were observed.Jaundice was present in 18 (7.6%) cases out of 240 children. these patients had tender hepatomegaly, elevated hematocrit, decreased platelet count, and deranged liver enzymes. The difference between variables is found to be statistically significant i.e 0.05 for liver profile in the study group. Stastistically significant

p value indicates liver derangement is more in severe dengue fever than compared with dengue fever with warning signs and dengue fever without warning signs.

Table 1 Liver profile in dengue fever

parameters	Dengue fever (130)	Dengue fever with warning signs (56)	Severe dengue (54)	P value ≤0.05(significant)
Serum Bilirubin	1 (0.76%)	4 (7.1%)	8 (15%)	0.0005
↑ALT	90 (69.6%)	44 (78.5%)	50 (92.3%)	0.0027
↑AST	110 (84.8%)	54 (96.4%)	52 (96.2%)	0.0097
ALP	63 (48.4%)	32 (57.14%)	41 (76.9%)	0.0028
Total protein	6.2	5.8	6.2	0.6
Albumin	3.3	3.2	3.3	0.9
Globulin	1.9	2.8	2.8	0.001
Prolonged APTT	2	8 (14.2%)	12 (22.2%)	1.8
↑INR	1	19 (33.9%)	26 (48.14%)	0.001

Table 2 Symptomatology in dengue fever

CLINICAL FEATURES	%	(n)
Fever	100 %	240
Myalgia	67 %	160
pain abdomen	57 %	136
Vomiting	40 %	96
Rashes	36 %	86
Petichiae	23 %	53
Jaundice	7.6 %	18

DISCUSSION

The extent to which the liver is affected by Dengue virus ranges from mild lesions to fulminant hepatitis.[10, 11, 12] Mechanisms of liver injury in dengue may be due to 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.[13,14,15,16,17]Reports have demonstrated a high affinity of the dengue virus for human liver cells and dengue virus has been isolated from the liver of fatal cases.

Out of 240 cases in our study, 79% had hepatomegaly which was more common in DHF (88.5%) and DSS (96%) group than in DF group.

The hepatic enzymes were elevated significantly in dengue fever with warning signs and severe dengue when compared to DF group which is similar to other studies [18].AST rise more than ALT in dengue may be due to involvement of myocytes.[18] This differs from the pattern seen in viral hepatitis, in which ALT levels are usually higher than or equal to AST levels.[18] we also observed that ALT was elevated in 69.6% cases of dengue fever, 78.8% of dengue fever with warning signs, 92.3% in severe dengue.

AST was elevated in 84.8% dengue cases, 96.4% dengue fever with warning signs cases, 96.2% severe dengue cases. Hypoalbuminemia and hypogammaglobulinemia was also observed. The reduction of serum globulin may be an important factor in fluid loss into third space which is indicative of severity of dengue infection. Elevated transaminase levels have been suggested as a potential marker to help differentiate dengue from other viral infections during the early febrile phase[20]

CONCLUSION

In dengue varying degrees of damage to the hepatic parenchyma, ranging from mild increases in aminotransferases to increases of up to 10 times the reference values. The use of liver tests to evaluate the degree of liver damage is of great importance, significant rise of liver enzymes helps in recognition of severe forms of dengue infection. Presence of fever, jaundice and hepatomegaly in endemic areas should arouse the suspicion of dengue hepatitis.

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