Section: General Medicine

Original Research Article

ASSESSMENT OF LIVER FUNCTION IN DENGUE FEVER

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Abstract

Background: Dengue fever is the most common arbovirus infection in the world. The incidence of Dengue has grown dramatically around the world in recent decades. WHO 2009 –"Dengue, Guidelines for Diagnosis, Treatment, Prevention and Control" classifies the spectrum of Dengue into Dengue fever(with or without warning signs) and Severe Dengue. This study was aimed at assessing the biochemical and clinical profile of hepatic involvement by Dengue virus. **Materials and Methods:** This was a teritiary care hospital based prospective observational study. All serologically positive Dengue cases, either Dengue NS1 antigen positive or IgM antibody positive cases from a teritiary care hospital in the study period are included in the study. After taking consent for the study, detailed history regarding previous attack of Dengue, chronic liver disease, hepatotoxic drugs etc was obtained. Clinical methods put emphasis on assessing the liver size, presence or absence of ascites, icterus and for signs of hepatic decompensation. **Result:** Around 70 Dengue cases were included in the study. According to the WHO 2009 guidelines for classification of Dengue fever the number of 'Dengue' cases in the study were 56 and the number of 'Severe Dengue' cases were 14. Bleeding manifestations were the main feature of the Severe Dengue cases. Liver involvement was seen in almost all cases. The most consistent abnormality that was observed was elevation of transaminases. All cases had normal liver enzymes on follow up. **Conclusion:** Liver involvement is common in Dengue fever, the most common manifestation being Dengue hepatitis. As repeated infections can cause severe disease, prevention of Dengue fever by an effective vaccine is of paramount importance.

INTRODUCTION

Dengue, one of the most rapidly spreading mosquito-borne viral diseases in the world, is an acute infection caused by an arbovirus in the Flavivirus genus, and the mosquito Aedesaegypti is the vector. The incidence of Dengue has grown dramatically around the world in recent decades. Over 2.5 billion people – over 40% of the world's population – are now at risk from dengue. WHO currently estimates there may be 50–100 million dengue infections worldwide every year.[1]

There are four distinct, but closely related, serotypes of the virus that cause dengue (DEN 1-4). Recovery from infection by one provides lifelong immunity against that particular serotype. However, cross-immunity to the other serotypes after recovery is only partial and temporary. Secondary infection, in the form of two sequential infections by different serotypes is also an epidemiological risk factor for severe disease.[2]

Reported case fatality rates for the South East Asia region are approximately 1%, but in India focal outbreaks away from the urban areas have reported case-fatality rates of 3-5%. In patients presenting with fever and hepatic dysfunction the diagnosis of Dengue should be strongly considered if the region is endemic for Dengue fever.[3] Hepatic dysfunction in dengue infection may be attributed to direct viral effect on liver cells or as a consequence of dysregulated host immune response against the virus. Although liver is not the main target for this disease histopathology findings include centrilobular necrosis, fatty alteration, hyperplasia of Kupffer cells, acidophil bodies and monocyte infiltration of portal tract. Even from India reports show dengue as a common cause of acute hepatic failure in pediatric age group especially during periods of epidemic.[4] However the scenario in adult population is not as well established and dengue is not usually considered as a differential diagnosis in patients of acute liver failure. In Kerala

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large scale studies are not yet conducted to assess the extent of liver involvement in Dengue fever.

MATERIALS AND METHODS

It was a Prospective Observational Study done in Medical ward and intensive care unit. 70 cases of Dengue fever admitted to the hospital during the study period

Inclusion Criteria

All serologically positive Dengue cases, either Dengue NS1 antigen positive or IgM antibody positive cases from Jubilee Mission Medical College in the study period are included in the study.

Exclusion Criteria

1. All Dengue fever positive patients with previously diagnosed chronic liver disease are excluded from the study.
2. All Dengue fever patients with previously diagnosed Hepatitis A, Hepatitis B, Hepatitis C and other hepatotropic virus infection are excluded from the study. All patients with previously diagnosed nephrotic syndrome and protein losing enteropathy are excluded from the study.
3. Children less than 12 years are excluded from the study
4. Those who do not consent are also excluded from the study

Methodology

All serologically positive Dengue fever cases, either Dengue NS1 positive or IgM Dengue positive are included in the study. Classification of cases into Dengue fever/Severe Dengue is based on the WHO criteria(Dengue guidelines, for diagnosis, treatment, prevention and control. New Edition. Geneva 2009). After taking consent for the study, detailed history regarding previous attack of Dengue, viral hepatitis, chronic liver disease, hepatotoxic drugs, nephritic syndrome, protein losing enteropathy and alcohol consumption is taken. Presence of rash, abdominal pain, headache, body pain and bleeding manifestations in the present episode are noted. Clinical methods put emphasis on assessing the liver size, presence or absence of ascites, icterus and for signs of hepatic decompensation. Liver function tests are performed at the time of admission, 5 days ,7 days and 2 weeks later or more frequently if abnormalities are detected. Biochemical and clinical assessment is also performed on subsequent follow ups in severe cases. Severe cases with marked elevation of enzymes are screened for hepatotropic viruses(Hepatitis B,Hepatitis C etc).Ultrasound Abdomen is also performed to look for gall bladder wall oedema,ascitis, liver and spleen size and to rule out chronic liver disease.The clinical profile in the two groups are compared and conclusions reached.

Statistical Analysis

The data obtained were entered into Microsoft Excel after coding for the variables. The master chart thus obtained is shown in the appendix along with the key. All analysis were carried out using the statistical software IBM SPSS version 20. Mean was used as the measure of central tendency and standard deviation was used as a measure of dispersion for descriptive statistics. Pearson Chi-square test and t-test were used to analyse the association between different variables depending on the type of variable. p value <0.05 was taken as statistically significant.

RESULTS

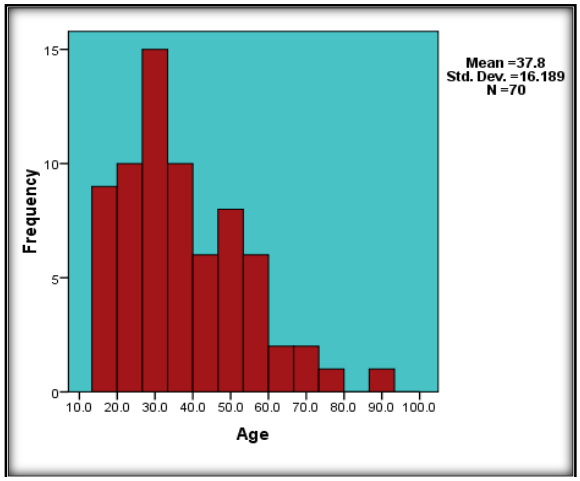

Figure 1: Age distribution of cases

As per figure 1 the mean age was 37.8±16.8 among the total sample size of 70 patients.

Table 1:

	DENGUE	SEVERE DENGUE
SGOT		
at presentation	140 (1.52)	246 (2.19)
7 days follow up	92 (83.2)	166 (258.3)
2 week follow up	29 (12.3)	40 (16.2)
SGPT		
at presentation	100 (1.07)	150 (1.30)
7 days follow up	73 (72.6)	155 (266.3)
2 week follow up	24 (16.7)	28 (10.36)

Table 2 (A) and (B)- Comparison of LFT between two Dengue types

BILIRUBIN		
at presentation	0.78 (0.39)	1.4 (1.12)
7 days follow up	0.8 (0.40)	1.35 (1.19)
2 week follow up	0.78 (0.77)	0.81 (0.40)
DIRECT BILIRUBIN		
at presentation	0.18 (0.16)	0.44 (0.41)
7 days follow up	0.2 (0.15)	0.51 (0.60)
2 week follow up	0.12 (0.12)	0.21 (0.12)
INDIRECT BILIRUBIN		
at presentation	0.59 (0.30)	1.04 (0.84)
7 days follow up	0.61 (0.31)	0.84 (0.55)
2 week follow up	0.53 (0.24)	0.70 (0.24)

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As per [Table 2 (A) and (B)] The mean SGOT and SGPT at presentation for Dengue fever was 140 and 100 respectively whereas for Severe Dengue it was 246 and 150 respectively. At 2 weeks of follow up the average SGOT and SGPT was 29 and 24 respectively for dengue fever whereas it was 40 and 28 for Severe Dengue. The average serum bilirubin at presentation for Dengue fever was 0.78 and 2 weeks followup showed 0.77. The average serum bilirubin at presentation for Severe Dengue was 1.4 and 2 weeks follow up showed 0.81. The average direct bilirubin at presentation was 0.18 for Dengue fever and 0.44 for Severe Dengue.2 week follow up showed average values of 0.12 and 0.21 for the two groups respectively. The average indirect bilirubin at presentation was 0.59 for Dengue fever and 1.04 for Severe Dengue.2 weeks follow up showed 0.70 for Dengue fever and 0.53 for Severe Dengue

Table 3: Total Count and Platelet Count comparisons

Total Count	Dengue	Severe Dengue
At presentation	4389(2931)	6143(6251)
On 7th day	5689(2232)	8246(6148)
At 2 weeks	6927(1446)	6749(3217)
Platelet count	**Dengue**	**Severe Dengue**
At presentation	106000(51100)	51100(34880)
On 7th day	143800(77765)	141300(69707)
At 2 weeks	266000(86663)	259400(69248)

As per [Table 3] the total count and platelet count comparison was seen in dengue and severe dengue patients it was seen as the time increases the count increases in both total and platelet count and it was statistically significant. ($p<0.05$)

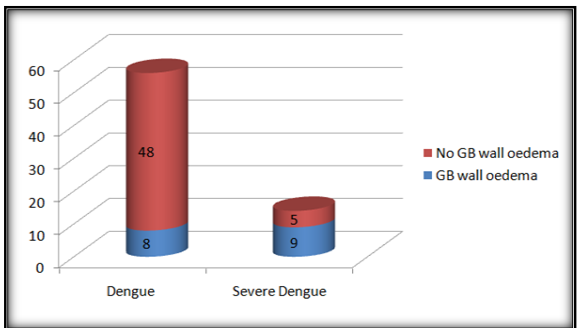

Figure 2: Gall Bladder wall oedema as assessed by Ultrasound scan

Gall bladder wall oedema in 14.3 % of Dengue fever and 64.3% of cases of Severe Dengue ($p<0.05$)

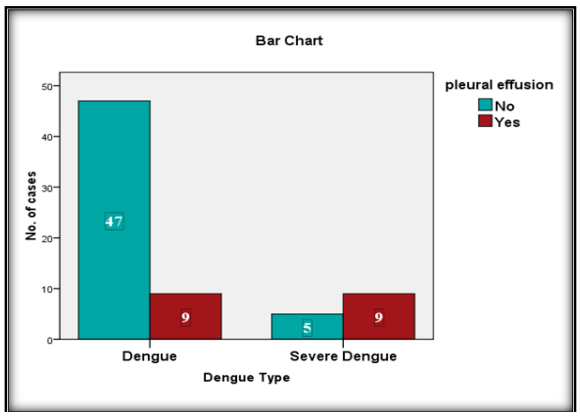

Figure 3: Pleural effusion observed in cases studied

Pleural effusion was also significantly higher in Severe Dengue when compared to Dengue fever.

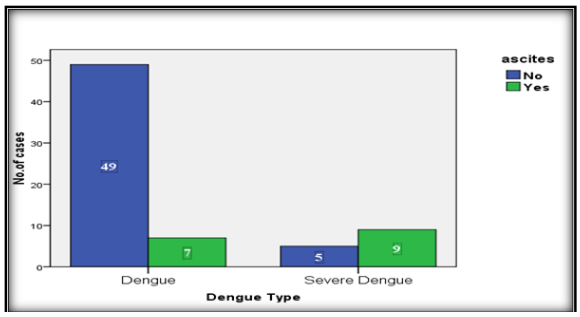

Figure 4: Ascites in the cases studied

Ascites was observed in 23% of all cases. Ascites was significantly higher in Severe Dengue when compared to Dengue fever.

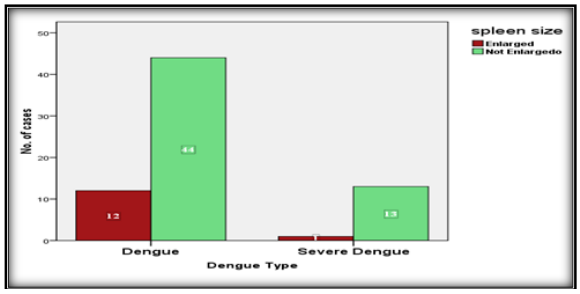

Figure 5: Spleen size as observed in cases

Splenomegaly as assessed by ultrasound was there in 18.6 % of total cases but was not significant between the groups. As assessed by ultrasound, pole to pole measurement of >12cm was taken as cut off for splenomegaly.

DISCUSSION

Liver involvement was seen in almost all cases. The most consistent abnormality that was observed was elevation of transaminases. Most of the cases were referred form outside hospitals as fever with low platelet count and elevated transaminases. A few cases were wrongly diagnosed as viral hepatitis from outside hospitals. None of the cases had fulminant hepatic failure. The transminases returned

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to the normal level in many cases before discharge. The liver enzymes were more elevated in Severe Dengue when compared to Dengue fever. All cases had normal liver enzymes on follow up. Similar results were seen in few studies which shows same involvement of transaminases.[5-8]

Even though 14% of cases presented with clinical icterus the bilirubin levels were normal in majority of cases. The liver dysfunction was not severe enough to affect the conjugatory functions of the liver. The bilirubin levels on follow up also remained normal. The was a slight increase in bilirubin levels in severe dengue cases when compared to Dengue fever this was consistent with the results of the study done in few studies.[9-11]

As per the blood parameters the prothrombin time was normal in all cases studied, both in Dengue fever and Severe Dengue cases. This points to the fact that bleeding manifestations were due to low platelet counts rather than to the altered coagulation profile seen in these patients. The synthetic functions of the liver were not affected in all these cases and was favored by few studies.[12,13]

Ascites and pleural effusion that was seen in 16 cases were due to the serositis rather than hepatic dysfunction. Pleural effusion was also significantly higher in Severe Dengue when compared to Dengue fever. Splenomegaly as assessed by ultrasound was there in 18.6 % of total cases but was not significant between the two groups. The study attempts to outline the liver involvement in a cohort of patients presented to a tertiary care teaching hospital. Many of the cases were referred from outside hospitals as fever with hepatitis and thrombocytopenia.[14,15] On subsequent evaluation theses cases proved to be Dengue fever. The study points to the fact that the liver involvement in Dengue fever is not severe in most of the cases and does not add to the morbidity and mortality.

CONCLUSION

The liver involvement measured in terms of elevation of transaminases was more for Severe Dengue when compared to Dengue fever. The previous studies also showed that Dengue hepatitis is severe in cases of Dengue hemorrhagic fever and Dengue shock syndrome. The bilirubin levels were high in Severe Dengue when compared to Dengue fever at presentation eventhough follow up did not show any significant difference between the groups.The coagulation parameters measured in terms of Prothrombin time had no significant difference between the groups. The occurrence of Ascites,Gall bladder wall odema and pleural effusion was more in Severe Dengue when compared to Dengue fever. Dengue hepatitis is a well known entity and this study attempts to outline the manifestations and correlate it with the severity of Dengue fever. The role and importance of a preventive Dengue vaccine lies in this aspect. If we are able to develop a cheap and effective vaccination for Dengue ,then we can prevent the occurrence of severe cases in the future. Further studies are required to assess the liver involvement in cases with repeated infection with Dengue virus.

REFERENCES

1. WHO. Dengue and severe dengue:Fact sheet. http://www.who.int (accessed 30 October 2014).
2. Nathan M B,Drager R D,Guzman M. Dengue-Guidelines for diagnosis, treatment, prevention and control. WHO. 2009.
3. Burke T. Dengue hemorrhagic fever: a pathological study. Trans R Soc Trop Med Hyg1968; 62(5): 682-692.
4. Roy A, Sarkar D, Chakraborty S, Chaudhuri J, Ghosh P. Profile of hepatic involvement by dengue virus in dengue infected children. North Amer J Med Sci2013; 5(8): 480-485.
5. Seneviratne SL, Malavigne GN, de Silva HJ. Pathogenesis of liver involvement during dengue viral infections. Trans R Soc Trop Med Hyg2006; 100(7): 608-614.
6. de Souza LJ,AlvesJG, Nogueira RM, Gicovate NC, Bastos DA, Siqueira et al. Aminotransferase changes and acute hepatitis in patients with Dengue fever. Braz J Infect Dis 2004; 8(2): 156-163.
7. Poovorawan Y, Hutagalung Y, Chongsrisawat V, BoudvilleI, Bock HL. Dengue virus infection:a major cause of acute hepatic failure in Thai children. Ann Trop Paediatr2006; 26(1): 17-23.
8. Kumar R,TripathiP,TripathiS,KanodiaA,Venkatesh V. Prevalence of dengue infection in north Indian children with acute hepatic failure. Ann Hepatol2008; 7(1): 59-62.
9. Gasperino J, Yunen J, Guh A, Tanaka KE, Kvetan V, Doyle H. Fulminant liver failure secondary to haemorrhagic dengue in an international traveller. Liver Int2007; 27(8): 1148-1151.
10. Kimura R, Hotta S. Studies on dengue fever (IV) on inoculation of dengue virus into mice. Nippon Igaku1944; 3379 : 629-33
11. Cherian.T, Ponnuraj E, Kuruvilla T, Kirubakaran C, John TJ, Raghupathy P. An epidemic of dengue haemorrhagic fever & dengue shock syndrome in & around Vellore. Indian J Med Res 1994; 100 : 51-6.
12. Dengue vaccine: WHO position paper – July 2016; Weekly epidemiological record; No 30, 2016, 91, 349–364
13. Stanaway JD, et al. The global burden of dengue: an analysis from the Global Burden of Disease Study 2013. Lancet Infect Dis. 2016 Jun; 16(6): 712–723.
14. Bell DJ. Fever in the returning traveller. The journal of the Royal College of Physicians of Edinburgh 2012; 42(1):43-46
15. Lanteri MC, Busch MP. Dengue in the context of “safe blood” and global epidemiology: to screen or not to screen? Transfusion 2012; 52(8): 1634–39.

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