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An Observational Study on Clinical and Liver Profile in Dengue Cases at a Tertiary Care Hospital in South India

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Abstract: Introduction: Dengue fever, the most common arthropod-borne viral illness in humans, is caused by the dengue virus, which is one of the world's most dangerous tropical infectious diseases. Dengue fever epidemics have been reported in India on various occasions. Liver involvement is known to occur in children with dengue fever. Liver dysfunction ranges from mild injury with elevated transaminase activity to severe injury with liver cell failure. Liver dysfunction varies in severity depending on the type of clinical presentation of dengue fever, but it is more common in children with severe dengue fever. Hence the following study was conducted to find out the range of liver dysfunction in children with dengue fever. Material and Methods: The study was conducted in a tertiary care hospital over a period of one year in a total of 100 patients who are serologically positive for dengue fever. Results: Patients were classified as dengue fever (DF)-48%, and dengue hemorrhagic fever (DHF)-52%. Liver function tests AST, ALT and ALP, bilirubin and albumin were deranged in children with dengue hemorrhagic fever. The mean total bilirubin, serum albumin, AST, ALT, ALP, PT, aPTT, INR, BT, CTwere 1.7 mg/dl, 2.9 mg/dl, 382 U/L, 240 U/L, 254.4 U/L, 39.8s, 56.8s, 1.5, 4.6 minutes and 2.5 minutes respectively. Derangement of liver function tests was significant among DHF as compared to DF. Conclusion: Liver dysfunction was very common in all forms of dengue fever, significantly deranged among DHF. AST levels raising significantly when compared to ALT.

Keywords: Dengue fever, Dengue hemorrhagic fever, Aspartate transaminase, Alanine Transaminase.

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INTRODUCTION

Dengue fever is still a major clinical and public health concern around the world. Dengue fever affects more than 2.5 billion people in the Tropics and Subtropics, each year an estimated 390 million cases were reported in roughly 125 countries [1, 2]. During the monsoon and post-monsoon seasons, the incidence of dengue epidemics increases. The demographics most affected are children and young adults. It's a mosquitoborne Arboviral disease spread by the Aedes mosquito.

Thrombocytopenia is one of the most prevalent test results in Dengue [3]. Apart from thrombocytopenia, hepatic dysfunction is known to occur in Dengue, manifesting either as pain in right hypochondrium, hepatomegaly, jaundice or elevated aminotransferases [4-6]. It can cause liver dysfunction as a result of a direct viral action on liver cells and Kupffer cells or as a result of a dysregulated host immunological response to the virus.

Pathophysiological changes involved here are viral cytopathy, hypoxic mitochondrial malfunction, immunological response, NV-induced TRAIL34, TNF, Fas signalling and increased endoplasmic reticular tension, finally leading hepatocyte to apoptotic phase. Severe types of Dengue fever had higher median Aspartate transaminase (AST) and also Alanine transaminase (ALT) values than uncomplicated Dengue fever. This could point to a link between higher transaminase levels and worsening disease severity. In contrast to the convalescent phase, the values of liver enzymes were shown to be higher in the febrile and severe phases of Dengue.

WHO (2009) Classification Dengue illness [7]:Undifferentiated fever

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- Dengue fever (DF)
- Dengue hemorrhagic fever (DHF)
- Subcategorized into 4 severity grades
- Grades III and IV are defined as Dengue shock syndrome (DSS)

Since liver involvement is so common in paediatric dengue cases this study has been conducted in a tertiary care hospital to know the severity of liver involvement by measuring Transaminases in Dengue fever and Dengue haemorrhagic fever.

MATERIALS AND METHOD

The hospital based study prospective observational study was conducted in a hundred patients with dengue fever to determine the profile of liver involvement in children with IgM positive Dengue viral infection.

Inclusion Criteria

- 1. Patients with serologically confirmed IgM positive Dengue viral fever.
- 2. Children between 1 to 12 years of age regardless of their gender.

Exclusion Criteria

- 1. Dengue-like diseases that are IgM negative
- 2. Children under the age of one year and above the age of twelve.
- 3. Children having a history of liver disease.

Data Collection

A proforma containing the sociodemographic data, history, symptoms was collected. The following investigations were done on the participants.

Complete blood counts, serum Dengue IgM, liver function tests such as serum bilirubin, AST, ALT, Alkaline phosphatase, total protein, serum albumin, prothrombin time and activated partial thromboplastin time were performed on all children enrolled in the study.

Informed verbal consent of the participants was taken. Ethical approval for conducting the study was obtained from Institutional Ethical Committee. Analysis was performed using the SPSS 12.0 software (SPSSInc., Chicago, IL USA)

All data are expressed as the mean ±SD or as frequencies and proportions. Differences in the demographic and clinical data between patients with DF and DHF were tested by the chi-square test. Differences in laboratory data between patients with DF and DHF were analyzed using the Student's t-test for continuous variables. A P- value less than 0.05 was considered significant.

RESULTS



Fig 1: Age wise distribution of participants



Fig 2: Gender distribution



Fig 3: Distribution based on Diagnosis

In the present study out of 100 participants majority belong to 5-9yr age group. Only 22% of the study population belong to 10-12 yr age group (Fig 1). The mean age of the study population was 6.52 ± 3.51 . In this study, near-equal distribution was observed among the study population in relation to gender. 54%

were female and 46% were males (Fig 2). Based on diagnosis, 52% were diagnosed as Dengue Haemorrhagic fever and 48% were diagnosed as Dengue fever (Fig 3). In this study, the mean age for the DF group was 6.16 ± 4.03 and the mean age for the DHF group was 7.32 ± 3.80 .

	Diagnosis		P value
	DF (n=48)	DHF (n=52)	
Age Mean ± SD	6.16 ± 4.03	7.09 ± 3.44	0.06
Fever	48 (100%)	52 (100%)	0.64
Headache	21 (43.75%)	35 (67.31%)	0.01*
Vomiting	24 (50%)	42 (80.77%)	0.01*
Pain abdomen	26 (54.17%)	44 (84.62%)	0.001*
Arthralgia	8 (16.67%)	15 (28.85%)	0.15
Malena	2 (4.17%)	15 (28.85%)	0.001*
Rash	41 (85.42%)	43 (82.69%)	0.71
Lymphadenopathy	41 (85.42%)	43 (82.69%)	0.15
Edema	12 (25%)	20 (38.46%)	0.15
Petechiae	25 (52.08%)	39 (75%)	0.01*
Hepatomegaly	46 (95.83%)	48 (92.31%)	0.46
Spleenomegaly	18 (37.5%)	29 (55.7%)	0.04*

Table 1: Demographic and clinical profile of DF and DHF groups

Chi-square test p<0.05

There was no statistically significant difference observed between the Diagnosis and Age distribution as the p-value was calculated to be >0.05. In this study, all the patients presented with fever, Headache was observed more among the DHF group (67.31%) compared to the DF group (43.75%). This finding was statistically significant as the p-value was calculated to be <0.05.

Vomiting was observed more among the DHF group (80.77%) in contrast to DF group (50%). This finding was statistically significant as the p-value was calculated to be <0.05.Pain abdomen was observed more among the DHF group (84.62%) in contrast to DF

group (54.17%). This finding was statistically significant as the p-value was calculated to be <0.05.

Malena was observed more among the DHF group (28.85%) in contrast to DF group (4.17%). This finding was statistically significant as the p-value was calculated to be <0.05. In this study, Based on signs and their comparison between the study groups, petechiae and splenomegaly were observed to be statistically significant as the p-value was calculated to be <0.05 (Table 1). No statistically significant finding was observed between the symptoms of Arthralgia, Rash, between the study groups as the p-value was calculated to be <0.05.

1 able 2: Bloch	P value		
	Diagnosis DF (n=48)	DHF (n=52)	
Hb	10.40 ± 2.30	10.11 ± 2.25	t value = 0.63
			P=0.52
HCT	32.10 ± 6.50	29.56 ± 6.86	t value = 1.89
			P=0.06
Platelets	1.76 ± 0.83	1.46 ± 0.77	t value $= 1.89$
			P=0.06
Total Bilirubin	0.79 ± 0.67	2.45 ± 0.15	t value = 17.40
			P=0.0001*
Direct Bilirubin	0.27 ± 0.58	1.47 ± 1.63	t value = 4.82
			P=0.0001*
Indirect Bilirubin	0.51 ± 0.13	0.99 ± 0.74	t value = 4.42
			P=0.0001*
S. Proteins	6.30 ± 0.83	5.82 ± 0.02	t value = 4.17
			P=0.0001*
Albumin	3.17 ± 0.52	2.70 ± 0.51	t value = 4.56
			P=0.0001*
AST	117.63 ± 124.56	626.04 ± 124.50	t value = 20.39
			P=0.0001*
ALT	76.40 ± 61.38	392.10 ± 61.14	t value = 25.74
			P=0.0001*
Alkaline phosphatase	181.52 ± 95.81	321.69 ± 95.75	t value = 194.07
			P=0.0001*
PT	16.64 ± 7.91	61.10 ± 7.80	t value = 28.28
			P=0.0001*
APTT	35.82 ± 7.99	76.12 ± 7.96	t value = 25.24
			P=0.0001*
INR	1.43 ± 0.74	1.64 ± 0.48	t value $= 1.69$
			P=0.09

Student t test p value<0.05

In this study, a statistically significant difference was observed between the study groups in relation to Total Bilirubin, Direct Bilirubin, Indirect Bilirubin, serum proteins, Albumin, AST, ALT, Alkaline Phosphatase, PT, APTT, BT as the p-value calculated to be <0.05 (Table 2).

DISCUSSION

Dengue fever, also known as "Break-bone fever," has become one of the most common causes of feverish disease in tropical and subtropical areas. Dengue fever is a mosquito-borne disease that is second only to malaria as one of the most common cause of Arboviral disease worldwide.

Age

In the study conducted by Jagadish Kumar K *et al.*, [8] the majority of the participants were aged around 5 years and by Carlos *et al.*, [9] the participants mean age was around 9.8 ± 4.0 years and by Dussart P *et al.*, [10] the participants mean age was 8.2 ± 3.3 years, these findings were in consonance with this study.

Gender

In the study conducted by Carlos *et al.*, [9] the male-female ratio was 1.49 and this was in close consonance with the present study.

Clinical Profile

In the study conducted by Carlos *et al.*, [9] the majority were cases of Dengue fever and 33.4% were cases of DHF and this distribution was in close consonance with the present study.

In the study conducted by Carlos *et al.*, [9] A significant increase in the frequency of abdominal pain was found among the DHF group before admission (P < 0.008) and at the time of admission compared with the DF group

Transaminases

Praveen M *et al.*, [11] reported that 100% of patients out of 60 participants had elevated AST and 85% patients had elevated ALT. The albumin level was low in 75% patients. Average AST was 316 units/L and average ALT was 156 units/L.

Mohan *et al.*, reported that AST and ALT levels were raised during the initial 1st and 2nd week,

respectively. In compared to conventional Dengue fever, hepatic impairment in the form of markedly increased enzymes was found to be more common in severe and complicated Dengue [12].

According to Kuo *et al.*, it was 93.3% [13] but as per Nguyen *et al.*, it was 97.7% [14] of Dengue infection cases had increased AST levels.

In a study by Sedhain *et al.*, liver enzyme SGOT was increased with the value of more than 50 IU/mL in 78.4% and 96.5% of cases of DF and DHF, respectively [15].

In a study by Gandhi *et al.*, (85%) of the patients had an elevation of at least one of the liver enzymes (P < 0.001) with alterations in SGOT [16].

According to Roy *et al.*, there was 84.4 percent and 93.75 percent ALT and AST elevation in DF with a warning sign, and 94.5 percent and 95.9 percent ALT and AST elevation in severe Dengue and acute hepatic failure in the severe Dengue group [17].

In a major study from Brazil, elevated AST and ALT levels were found in 63.4 percent and 45 percent of patients, respectively, out of 1585 Dengue cases, with 3.8 percent of cases having a 10 fold higher in transaminase level. Other authors have reported a similar increase in liver enzymes of more than 10 fold in adults, ranging from 1.8% to 11.2% respectively, had elevated AST and ALT levels [18].

Petdachai *et al.*, reported that levels of AST were higher than those of ALT [19].

In our study 44 percent of DSS, 22.8 percent of DHF, and just 3.4 percent of the DF group, we detected a higher than 10-fold increase in AST. This study found a more than 10-fold increase in ALT in 16 percent of DSS, 7.7% of DHF, and 0% of DF participants. Transaminases levels were found to be more than 10 times higher in the DSS and DHF groups than in the DF group, which was statistically important.

In the current investigation, most of our patients exhibited elevated liver enzymes with SGOT values being higher than SGPT values, as in previous studies. Hepatic enzyme impairment was more common in patients with severe Dengue.

CONCLUSION

Dengue is one of the most common viral illness in India, significantly affecting paediatric population. Among children liver is one of the common organ that is affected ranging from elevated Transaminases to Liver cell failure depending on severity of Dengue illness. Among those with Dengue haemorrhagic fever Transaminases especially AST when compared to ALT and ALP is one which is significantly elevated when compared to Dengue fever.

Elevated serum bilirubin and coagulation profile (PT, aPTT, INR) with increased incidence and severity of vomitings, abdominal pain, spleenomegaly, petechiae and malena are significantly associated with DHF than DF.

Elevation of Transaminases specifically AST and these clinical symptoms can be taken as early predictors for progression into DHF in order to prevent mortality in paediatric population by early commencement of appropriate supportive care especially in those with liver involvement [20, 21].

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