ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 7 | July - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

LIVER DYSFUNCTION AND DENGUE- A HOSPITAL BASED STUDY IN JHARKHAND

Medicine

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ABSTRACT

Dengue is one of the most common arboviral diseases in the world. It is caused by a mosquito borne flavivirus, a single stranded positive sense RNA virus. Dengue related hepatic dysfunction is a huge burden on the healthcare system of tropical and subtropical countries. Although majority of cases recover spontaneously, a small fraction may progress to acute liver failure and death. The aim of the study was to analyse the liver function tests in serologically proven dengue patients. ***Materials and Methods:*** 150 patients admitted with confirmed Dengue status (IgM/NS1 positive) in our hospital were included in this study and their liver function tests were studied. ***Results:*** ALT was normal in 15.3% cases, upto 2 fold increase in 32 % cases, 2-4 fold increase in 28.7% cases, 4-10 fold increase in 18.7% cases and more than 10 fold increase in 5.3% cases. Serum AST levels were found to be normal in 3.3% cases, upto 2 fold increase in 31.3% cases, 2-4 fold increase in 32% cases, 4-10 fold increase in 25.3% cases while more than 10 fold increase in 8% cases. PT was elevated in 10.6% cases and PTT was found to be elevated in 8% cases.

KEYWORDS

Dengue, ALT, AST, liver dysfuction

INTRODUCTION

Dengue is the most common mosquito borne arboviral disease in the world. Dengue virus is transmitted by female mosquitoes mainly of the species Aedes aegypti and, to a lesser extent, Aedes albopictus. Globally, 3.9 billion in 129 countries are at risk of Dengue virus infection[1] with 70% of the actual burden in Asia [2]. India is facing a problem of huge magnitude with yearly outbreaks in most of the Northern and Northeastern states [3] [4].

Table 1: WHO classification of Dengue

CRITERIA FOR DENGUE ± WARNING SIGNS		CRITERIA FOR SEVERE DENGUE
Probable Dengue	warning signs:	**Severe plasma leakage** leading to:
Fever and any 2 of the following: • Nausea, vomiting • Rash • Aches and pains • Tourniquet test positive • Leukopenia • Any warning sign	• Abdominal pain or tenderness • Persistent vomiting • Clinical fluid accumulation • Mucosal bleed • Lethargy, restlessness • Liver enlargment >2 cm • Laboratory: increase in HCT concurrent with rapid decrease in platelet count	• Shock (DSS) Fluid accumulation with respiratory distress **Severe bleeding** as evaluated by clinician **Severe organ involvement** • Liver: AST or ALT >=1000 • CNS: Impaired consciousness Heart and other organs

According to WHO 2009 classification [5] , dengue has been classified into dengue with and without warning signs and severe dengue. However, majority of studies classify dengue into Dengue fever, Dengue haemorrhagic fever and Dengue shock syndrome [6].

Severe dengue with its complications may ensue following endothelial injury and leakage of plasma. The present study is to analyse liver function tests in patients with Dengue.

METHOD

This study was a cross-sectional study done in a tertiary care hospital in Jharkhand. All patients above 15 years of age with confirmed Dengue status (NS1 and/or IgM positive) between August 2019- January 2020 were included in this study. Patients with co-infections like Malaria, Typhoid, Chikungunya, Leptospirosis, scrub typhus and pre-existing liver disease were excluded from the study. Serum ALT and AST was done using IFCC method, serum bilirubin was performed using DCA method, Alkaline phosphatase using IFCC, serum Albumin using Biuret method, Dengue IgM antibody detection using MAC-ELISA method, NS1 antigen detection using ELISA.

RESULTS

All the patients underwent liver function tests. ALT was normal in 15.3% cases, upto 2 fold increase in 32 % cases, 2-4 fold increase in 28.7% cases, 4-10 fold increase in 18.7% cases and more than 10 fold increase in 5.3% cases. Overall 15.3% cases had normal values while in 84.7% cases ALT was found to be deranged (Table 1).

Table 1: Alanine aminotransferase levels in Dengue patients (N=150)

ALT (Iu/L)	DF		DHF		DSS		Total	
Normal (<45)	21	17.9%	2	7.4%	0	0	23	15.3%
46-90	36	30.7%	10	37%	2	33.3%	48	32%
91-180	36	30.7%	6	22.2%	1	16.6%	43	28.7%
181-450	21	17.9%	6	22.2%	1	16.6%	28	18.7%
>450	3	2.5%	3	11.1%	2	33.3%	8	5.3%
	117		27		6		150	

Serum AST levels were found to be normal in 3.3% cases, upto 2 fold increase in 31.3% cases, 2-4 fold increase in 32% cases, 4-10 fold increase in 25.3% cases while more than 10 fold increase in 8% cases. Overall, AST levels were normal in 3.3% cases and elevated in 96.7% cases.

Table 2: Aspartate aminotransferase levels in Dengue patients(N= 150)

AST (Iu/L)	DF		DHF		DSS		Total	
Normal <45	4	3.4%	1	3.7%	0	0	5	3.3%
46-90	41	35%	5	18.5%	1	16.6%	47	31.3%
91-180	35	29.9%	12	44.4%	1	16.6%	48	32%
181-450	29	24.7%	6	22.2%	3	50%	38	25.3%
>450	8	6.8%	3	11.1%	1	16.6%	12	8%
	117		27		6		150	

Normal range of serum bilirubin is 0.3-1.1mg/dl.

Serum bilirubin levels were found to be elevated in 6% cases while Hypoalbuminemia (S. albumin < 3.5 g/dl) was seen in 8% cases. Alkaline phosphatase was elevated in 20.6% cases in our study.

Table 3- Percentage of cases with Hyperbilirubinemia and Hypoalbuminemia (N=150)

	Frequency	Percentage (of total 150)
S. bilirubin (> 1.2mg/dl)	9	6%
S. albumin (< 3.5g/dl)	12	8%
Alkaline Phosphatase (>200Iu/L)	31	20.6%

Hypoalbuminemia was seen in 3.3% cases of Dengue fever, 22% cases of Dengue Haemorrhagic fever and 40% cases of Dengue Shock Syndrome.

TABLE 4 - S. ALBUMIN LEVELS IN DF, DHF AND DSS

S.ALB (mg/dl)	DF		DHF		DSS	
	No.	%	No.	%	No.	%
<3.5	4	3.389%	6	22.22%	2	40%
>3.5 (NORMAL)	114	96.610%	21	77.77%	3	60%
Total	118	100%	27	100%	5	100%

TABLE 5- AST/ALT ratio in DF, DHF and DSS

AST/ALT ratio was found ≥2 in 12.5% cases in our study.

AST/ALT	DF	DHF	DSS
≥2	13 (8.6%)	4 (2.6%)	2(1.3%)

TABLE 6 – PT/PTT in DF, DHF AND DSS

	DF		DHF		DSS		TOTAL	
	PT	PTT	PT	PTT	PT	PTT	PT	PTT
Normal	112 95%	113 95.8%	18 66.7%	21 77.8%	4 80%	4 80%	134 89.3%	138 92%
Prolonged	6 5%	5 4.2%	9 33.3%	6 22.2%	1 20%	1 20%	16 10.7%	12 8%
Total	118 100%	118 100%	27 100%	27 100%	5 100%	5 100%	150 100%	

PT was prolonged in 5%, 33.3%, 20% cases in Dengue fever, Dengue haemorrhagic fever and Dengue shock syndrome respectively. In total, PT was elevated in 10.6% cases. PTT was prolonged in 4.2%, 22.2%, 20% cases in Dengue fever, Dengue haemorrhagic fever and Dengue shock syndrome respectively. In total, PTT was elevated in 8% cases.

DISCUSSION

Liver dysfunction is an important part of Dengue viral infection. The virus replicates in both the hepatocytes and Kupffer cells [7] [8]. The spectrum of liver involvement ranges from asymptomatic elevation of aminotransferases to acute liver failure. Hepatomegaly and elevated liver enzymes suggest liver involvement. Various symptoms seen are abdominal pain, vomiting, anorexia [9]. Hepatomegaly is seen in both dengue fever (DF) and DHF but it is more common in DF [10]. Also, hepatomegaly is seen more commonly in children than adults [11].

In majority of cases AST is more elevated than ALT, more during early phase of infection during the first week then declining to normal levels by three weeks.

In a study conducted by Shamsunder et al[12], Deshwal et al[13] and Tahlan et al[14] AST and/or ALT (>45IU/L) was observed in 66.6%,88.54% and 47.6% respectively. In a study by Gandhi et al [15], AST was elevated in 85% cases while ALT was elevated in 77.8% cases. In the present study AST (>45IU/L) was seen in 96.7% while ALT was elevated in 74.7% cases. Hence, this study confirmed the involvement of liver in Dengue as previously documented by various studies in the SEAR. In the present study most patients had elevated AST levels. Similar trend has been reported in other previous studies.

In a study by Amit et al [16], with regards to AST levels it was shown that 45.6% had less than 3 fold elevation, 36.7% had 3-10 fold elevation and 16.4% had greater than 10 fold elevation.10. In the same study with regards to ALT, 27.8% had 1-3 fold elevation, 59.4% had 3-10 fold elevation and 8.9% had greater than 10 fold elevation.

Wong et al reported that AST abnormality was higher as compared to ALT [17].In this study AST elevation was more than ALT which was similar to our study. Souza et al also reported a similar trend of AST and ALT elevation in dengue [18]. In our study, AST/ALT ratio was more than 2 in 12.5% cases.

The reversal of ALT/AST ratio is helpful to differentiate Dengue fever from other causes of acute viral hepatitis like HAV, HBV,HCV etc except Alcoholic hepatitis [19]. The median AST and ALT values have been found to be higher in severe forms of dengue than in uncomplicated Dengue fever [17] [18].

Parkash et al [20] and Larreal Y et al [21] in their study had reported hyperbilirubinemia in 3.1% cases which was comparable to our study which had hyperbilirubinemia in 6% cases. In a study by Narasimhan et al [22] alkaline phosphatase was elevated in 25% cases while in our study it was elevated in 20.6% cases.

Fernando et al [23] reported low serum albumin in 54.5% of cases. Saha et al reported low albumin in 12.9% of the cases [10] which was similar to the study reported by Wong et al which showed hypoalbuminemia in 16.5% cases [17]. In our study, Serum albumin was low in 8% cases. et al reported hypoalbuminemia in 71% of cases with dengue haemorrhagic fever [24] while in our study 22% cases of Dengue haemorrhagic fever had hypoalbuminemia.

Bashir et al [25] reported prolonged PT in 9% cases and prolonged PTT in 12.6% cases. In the present study, PT was prolonged in 10.6% cases while PTT was prolonged in 8% cases.

CONCLUSION

Liver dysfunction is an important part of dengue and therefore LFTs should be used routinely as a part of investigative studies in patients with dengue fever. Prolonged PT/PTT in dengue indicates impairment of the coagulation cascade and is indicative of progression to severe dengue. Serial monitoring of these parameters is important to predict the severity of dengue and help in early management.

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