



## Severity of Liver Involvement in Children with Dengue Infection

Afsana Yasmin<sup>1</sup>, Rozina Akhter<sup>2</sup>, Shahina Pervin Shapla<sup>3</sup>, Laila Yeasmin<sup>4</sup>

<sup>1</sup>Registrar, Department of Paediatrics, Dr. Sirajul Islam Medical College and Hospital, Dhaka, Bangladesh; <sup>2</sup>Associate Professor, Department of Paediatrics, Dr. Sirajul Islam Medical College and Hospital, Dhaka, Bangladesh; <sup>3</sup>Associate Professor, Department of Paediatrics, Dr. Sirajul Islam Medical College and Hospital, Dhaka, Bangladesh; <sup>4</sup>Professor & Chairman, Department of Paediatrics, Dr. Sirajul Islam Medical College and Hospital, Dhaka, Bangladesh

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### Abstract

**Background:** Liver involvement in dengue infection is one of the clinical presentations. **Objective:** This study was undertaken to see severity of liver dysfunction in children with dengue infection. **Methods:** It is a cross sectional observational study conducted in 100 consecutive children with serologically positive dengue infection aged between 2 months to 14 years of age. Liver function tests were done in all patients and were studied the severity of deranged LFT with severity of dengue infection. **Results:** Out of 100 admitted children with dengue infection, deranged liver function tests found in 57(57.0%). ALT was above normal in 10 (29.4% of DF, 19 (57.6%) cases of DHF and 19(57.6%) cases of DSS respectively. AST was above normal level in 12(35.3%) cases of DF, 23(69.7%) cases of DHF and 22(66.7%) cases of DSS respectively. Low albumin was found in 41.0% of cases, 15(45.5%) cases of DHF and 19(57.6%) cases of DSS. INR was high only 4 cases of DSS. The bilirubin was normal in all cases except one died due to ALF due to DSS. The mean ALT and mean AST statistically higher in DHF and DSS in compare to DF (P-value 0.011 and 0.037) respectively. However, there was no significant difference in meal ALT and AST between DHF and DSS respectively. Overall mortality in 2 cases with DHF and DSS. **Conclusion:** Dengue infection is associated with variable level of liver dysfunction. The severity of liver dysfunction can predict the severity of dengue infection. [*Bangladesh Journal of Infectious Diseases, December 2020;7(2):90-94*]

**Keywords:** ALT; AST; children; dengue infection; acute liver failure

**Correspondence:** Dr. Afsana Yasmin, Department of Paediatrics, Dr. Sirajul Islam Medical College and Hospital limited, Dhaka-1000, Bangladesh; Email: [afsanapgn@gmail.com](mailto:afsanapgn@gmail.com)

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## Introduction

Dengue virus infection continues a major health problem in large part of world<sup>1</sup>. The maximum burden of which is borne by the countries of the Asia-Pacific-Region<sup>2</sup>. The presentation of dengue viral illness is diverging from asymptomatic subclinical infection to severe multiorgan involvement and death<sup>3</sup>. Liver involvement in dengue infection is a well-known feature, ranging from mild to moderate elevation of serum transaminases to fulminant liver failure<sup>4-9</sup>.

The last severe outbreak occurred in Bangladesh from May to November 2019. A total 100 107 cases and 129 deaths have been officially documented by the government surveillance systems with a clear predominance of cases and fatalities during the summer months (July to November)<sup>10</sup>. DENV 3 was reported is cause of this outbreak of dengue infection in 2019<sup>11</sup>. This study was undertaken to see the severity of liver involvement with dengue illnesses in children.

## Methodology

This cross-sectional observational study was conducted in a tertiary care hospital of Dhaka, Bangladesh. A total 100 consecutive children with serologically diagnosed dengue infection aged 2 months to 14 years admitted in pediatric ward and PICU since 25<sup>th</sup> June to 25<sup>th</sup> July 2019 was included this study. Data was collected in preformed data collection sheet prospectively. Dengue infection was diagnosed by high-grade fever for few days and serologically confirmed by positive NS1 antigen or IgM ELISA. The laboratory tests like CBC, liver function test, creatinine, electrolytes, calcium and CRP done in all cases. Blood for culture sensitivity was also done in suspected cases of secondary bacterial infection. CXR and ultrasonogram of whole abdomen were done to see, pleural effusion, consolidation and ascites. The study population was divided into three groups Dengue fever (dengue infection without complications, Dengue Hemorrhagic fever (DHF) and dengue shock syndrome (DSS) according to WHO guideline. At the end of study data were analysed by SPSS for

Windows version 22. Descriptive statistics were used for demographic and baseline data and were presented as mean  $\pm$  standard deviation (SD), number or percentage. Chi-square test was used for categorical variable. P values  $<0.05$  was considered as significant.

## Results

A total 100 consecutive children with dengue virus infection was included in this study. All patients were serologically confirmed dengue, dengue NS1 was positive in 86 (86.0%) children and IgM ELISA positive in 14(14.0%) children. Of these 100 children, 58 were male and 42 were female. The study included 27 children below 5 years, 51 children between 5 to 10 years and more than 10 years 22 children.

**Table 1: Clinical and Laboratory Manifestations of Study Population**

Manifestations	Frequency	Percent
Fever for 1-5 days	100	100
Headache, Body aches	60	70
Nausea, Vomiting, Abdominal Pain	66	66
Petechiae, Purpura, Mucosal Bleeding	20	20
hepatomegaly	10	10
Ascites	14	14
Pleural Effusion and /or Consolidation	36	36
Leukopenia(<4000/cum m)	8	8
Thrombocytopenia (<1.5 lac)	80	80
<30000	25	25
30000-<50000	20	20
50000- <1 lac	27	27
1 lac-1.5 lac	8	8
Hypocalcemia	19	19
Dyselectrolytemia		
• Hyponatrinemia	8	8
• Hypokalemia	28	28
Hypoalbuminemia	41	41

Among the study population, 34 were diagnosed as dengue fever, 33 were dengue haemorrhagic fever and 33 were dengue shock syndrome. The

patients were presented with fever, anorexia, vomiting, abdominal pain, headache, body ache,

myalgia and bleeding manifestation. Imaging findings suggestive of ascites in 14 patients and

**Table 2: Liver Dysfunction in Dengue Fever**

Parameters	DF N(34)	DHF N(33)	DSS N(33)
ALT			
• Above Normal (>45U/L)	10(29.4%)	19(57.6%)	19(57.6%)
• > 10 times of normal	0(0%)	5(15.2%)	4(12.1%)
AST			
• Above Normal (> 45 U/L)	12(35.3%)	23(69.7%)	22(66.7%)
• > 10 times of normal	0(0.0%)	6(18.2%)	5(15.2%)
Albumin Low	7(20.5%)	15(45.5%)	19(57.6%)
INR high	0(0.0%)	0(0.0%)	4(12.1%)

pleural effusion and or consolidation was present in 36 children. Leukopenia, Thrombocytopenia, Hypocalcemia, Hypoalbuminemia and Dyselectrolytemia were found in 8, 80, 19, 41 and 36 children respectively. Serum creatinine was high only in 3.0% of patient. Lowest platelet below 30000 was found in 25 children. Two cases had died. One was a 3.5 years old boy a case of DSS with acute liver failure. His bilirubin 5.9 mg/dl, ALT was 3073 and AST 3670, INR 2.7, albumin 2.5, creatinine 1.3 mg/dl and lowest platelet 28000 per cumm. Other one was a 3 years old boy case of DHF with acute liver failure with hepatic encephalopathy stage IV. His bilirubin 0.7 mg/dl, ALT 1213 and AST 3820, INR 1.8, alb 3, platelet 21000, CRP high and blood c/s staphylococcus positive. Blood culture was positive in another patient who was improved.

We have done liver function test in all patients. Mean ALT (216 U/L) is lower than mean AST (281 U/L) in dengue fever. We found deranged LFT more common in DHF and DSS than classical DF. The ALT more than 10 times of normal in (15.2%) in DHF and 12.1% in DSS respectively. The AST more than 10 times of normal in 18.2% in DHF and 15.2% in DSS respectively. The hypoalbuminemia was also common in DHF and DSS. The bilirubin was high only in 3 patients (Table 2).

Table 3 showed that there was statistically significant difference in mean ALT and mean AST in between DF and DHF and DF and DSS. However, there was no significant difference regarding mean ALT and AST between DHF and DSS.

**Table 3: Difference of mean ALT and AST between DF and DHF and DF and DSS**

Parameters		Mean ( $\pm$ SD)	P value
ALT	DF	59.6( $\pm$ 73.4)	0.011
	DHF	242.4( $\pm$ 383.6)	
AST	DF	68.5( $\pm$ 80.7)	0.037
	DSS	383.8( $\pm$ 815.4)	
ALT	DHF	242.4( $\pm$ 383.6)	0.495
	DSS	348.6( $\pm$ 801.5)	
AST	DHF	383.8( $\pm$ 815.4)	0.946
	DSS	398.4( $\pm$ 901.9)	

## Discussion

At present, Dengue is the most rapidly spreading arboviral disease in the world. Approximately, 390 million dengue infections occur annually<sup>12</sup>. In Indian subcontinent, the pattern of dengue infection changes for last few decades from sporadic to endemic form<sup>13</sup>. The dengue circumstances in Bangladesh were getting worse in the year 2019<sup>14</sup>. Varying degree of acute liver injury is common in dengue viral infections, but does not associate with the degree of viraemia or the onset or extent of fluid leakage. Dengue associated liver injury appears to peak around day

6 and 7 or onwards<sup>15</sup>. The degree of liver dysfunction in children with dengue infection varies from mild injury with elevation of transaminases to severe injury with jaundice and acute liver failure. The manifestations of liver involvement such as nausea, vomiting, pain in the right hypochondrium, hepatomegaly, varying degrees of jaundice and an increase in liver markers principally AST and ALT. The previous studies showed liver dysfunction is more common in DSS and DHF than classical dengue fever<sup>16-21</sup>. Previous studies also showed, acute liver failure might occur in severe dengue fever and without intervention fatality rate high<sup>22-24</sup>.

The present study showed 66% of dengue children are DHF and DSS. ALT elevated in 57.6% and 57.6% in DHF and DSS respectively. AST elevated 69.7% and 66.7% in DHF and DSS respectively. ALT and AST also elevated in DF in 29.4% and 35.3% respectively. ALT and AST are very high more than 10 times of normal in DHF and DSS but none increases such level in DF. Mean ALT and AST significantly higher in DHF and DSS in compare to DF.

DeSouza<sup>7</sup> and colleagues observed alterations of AST and ALT levels in 63% and 45% of patients' respectively. They noted that the average levels of AST and ALT were significantly higher in DHF and DSS patients than in DF patients, an observation supported by other studies. Findings are almost similar with the present study. Mean AST level is higher than mean ALT which is opposite in viral hepatitis.

Bilirubin is high only in 3 patients in this study. Fernando S et al also found in their study cohort, only 2 pts had elevated bilirubin as cholestasis or biliary stasis, did not significantly occur in dengue associated liver disease<sup>15</sup>. Hypoalbuminemia is common in DHF and DSS<sup>15</sup>. The present study also found 15 and 19 children had hypoalbuminemia in DHF and DSS respectively. Low albumin is usually occurring due to severe liver dysfunction from hypovolumic ischemia or direct viral attack or cytokine mediated injury<sup>25</sup>. INR is high in 4 children with dengue infection.

Laoprasopwattana et al<sup>22</sup> showed in Thai children 1.1% children with dengue virus infection developed acute liver failure and among the ALF cases 68.3% had died. In the present study of

small cohort, we also found 2 % children developed liver failure. One DSS and another DHF with hepatic encephalopathy stage IV and both have died. One of them was superadded with secondary bacterial infection. Profound shock with multiorgan failure, especially involving respiratory failure and/or active bleeding, may be the major cause of death in patients with ALF<sup>25-27</sup>. Along the liver dysfunction, other complications are found like leucopenia, thrombocytopenia, hypocalcemia, dyselectrolytemia, lung consolidation, pleural effusion, and ascites. One case also developed cardiac complication like myocarditis and arrhythmia. Early recognition of myocardial involvement in dengue illness, prompt restoration of hemodynamic instability while avoiding fluid overload, and sparing unnecessary invasive management are important in treating dengue-affected patients with severe myocarditis<sup>26</sup>. The limitation of the study are small sample size.

## Conclusion

Liver dysfunction is common in children with dengue virus infection. It may be mild hypertransaminemia to fulminant liver failure. AST level is higher than ALT in dengue infection. Hypoalbuminemia also common in dengue infection may aggravate shock. Jaundice is unusual until development of cholestasis or severe liver failure. Acute liver failure along with encephalopathy or bleeding may causes death. Therefore, early diagnosis and prompt intervention can prevent complications and death.

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