

# Hepatic Dysfunction in Children Suffering from Dengue Fever

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## Abstract

**Background:** Dengue infections are associated with liver involvement leading to the occasional occurrence of liver failure of severe variety and even death. Dengue is almost endemic throughout India and it is much more serious and deleterious in children. We have, therefore, tried to estimate the prevalence of derangement of liver function in children affected with dengue virus infection.

**Materials and Methods:** This study was done in admitted dengue patients in our medical college in the age group of 1 month–12 years. Only 81 children of NS1 positive for dengue virus were included in the study. In all of these complete blood count and liver function tests were performed on the day of admission and every alternate date as long as they were admitted.

**Results:** All the parameters that are serum glutamic-oxaloacetic transaminase (SGOT), serum glutamate-pyruvate transaminase (SGPT), and gamma glutamyl transferase (GGT) raised throughout the whole period of dengue illness and the serum albumin level were reduced. However, these changes were most marked on the 5<sup>th</sup>–6<sup>th</sup> days of fever after which they again slowly waned.

**Conclusion:** Dengue fever causes hepatic injury in children, which is reflected by raised SGOT, SGPT, and GGT and reduced serum albumin. More the severity of the dengue infection more pronounced are the changes in liver derangement.

**Key words:** Dengue in children, Hepatic dysfunction, Severe dengue

## INTRODUCTION

Dengue is an infectious febrile disorder caused by an arbor virus belonging to the genera of single standard enveloped RNA viruses. Dengue virus has four serotypes (DENV 1–4) and is a member of Flaviviridae family and the genus *Flavivirus*.<sup>[1]</sup> In recent years, dengue fever has come as an important epidemic in many parts of the world and has been a menacing name in India also. It has now probably superseded the number of incidences of malaria and is at present, bearing a huge number of sufferers throughout the world, the annual incidences of dengue being more than a million in a year spreading over 125 countries.<sup>[2]</sup>

Regarding the complications of dengue, we generally mean dengue hemorrhagic fever and dengue shock syndrome. However, the occurrence of hepatic involvement in dengue is neither or less significant nor of any rare occurrence. In fact, involvement of liver complications in dengue is quite frequent and of quite serious consequences also, often leading to acute hepatic failure and even coma or death.<sup>[3,4]</sup> This is more of significance in children affected by dengue.

The common sequelae of hepatic failure from any cause (e.g, hepatitis A, B, or C) are: Acute liver failure leading to shock, coma, or even death; more chronic causes such as cirrhosis of liver, portal hypertension, hepatic encephalopathy, hepatorenal syndrome, and even cardiac failure. These all can occur following hepatic involvement as a consequence of dengue. Therefore, mortality due to hepatic involvement of dengue is quite high.

Shock is generally considered as the cause of liver failure in dengue but the same can occur even without any occurrence of shock.<sup>[5]</sup> Therefore, it is important to

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understand and assess the exact causes of liver failure in dengue. This is all the more important in case of children as they are the more vulnerable population and also for other obvious reasons. Apart from shock the other causes attributed in liver failure are direct attack of dengue viruses on hepatocytes, hypoxic damages of liver cells, and also immune-mediated apoptosis.<sup>[6]</sup> With all these facts in hand, we have tried to estimate the morbidity features of hepatic involvement of dengue fever in children.

## MATERIALS AND METHODS

### Study Place

The study was conducted on admitted pediatric dengue patients in a medical college hospital in the mid part of Bengal. In all of them complete blood counts (CBC), liver function tests (LFT), and other test for dengue (IgM and IgG) were performed. CBC and LFT were repeated on every alternate dates as long as they were admitted.

### Period of Study

The study was conducted over a period of 1 year 3 months, i.e., March, 2018–June 2019

### Inclusion Criteria

The following criteria were included in the study:

1. Serologically confirmed (NS1 ELISA and/or IgM MAC ELISA positive) dengue fever patient admitted to the department of pediatrics of our medical college
2. All cases in the pediatric age group (>1 month–12 years) were included irrespective of gender
3. Informed consent from parents and guardians were taken before undergoing the study.

### Exclusion Criteria

The following criteria were excluded from the study:

1. Children with pre-existing liver diseases
2. Those patients (parents/guardians) who refused to take part in the study.

### Sample size

In total, 81 patients were included in the study.

### Study parameters/variables

- I. Age
- II. Gender
- III. Urban/Rural
- IV. Dengue serological test (NS1 ELISA and/or IgM MAC ELISA done in the department of microbiology)
- V. Complete hemogram including platelet count (done in the department of pathology)
- VI. Liver function test (By LFT we mean serum bilirubin and its fractions, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase [ALP],

gamma-glutamyl transferase [GGT], total protein, albumin, and globulin).

### Study design

This study was conducted at institute based cross-sectional study.

### Study tools

- 1) Preformed history sheet to record the above-mentioned parameters
- 2) Laboratory test results
- 3) Bed-head-ticket of the patient.

### Study technique

NS-1 Ag and/or MAC ELISA for anti-dengue IgM specific antibodies in all fever cases in the said age group admitted in the pediatric medicine ward of our medical college and hospital during the specified study period for MAC ELISA history of fever should be 5 days or more and features suggestive of dengue.

Cases diagnosed as dengue positive when — detection of IgM antibody in single serum sample and/or NS-1 antigen positive for dengue virus.

Among the patients identified by the above technique as dengue positive cases, only those meeting the inclusion criteria of the study and consenting to take part in the study were included in the final study.

### Analysis of Data

Data were collected, recorded, and compiled on Microsoft Excel 2007 datasheet. After the end of the study, all the data were compiled, tabulated, and statistically analyzed, and inferences drawn.

## RESULTS

Out of total 81 dengue patients, 8 (9.88%) patients were diagnosed as severe dengue. Age-wise distribution of

**Table 1: Age-wise distribution of dengue cases**

Age in years	PD	D+WS	SD	Total
<1	-	1	1	2
1–2	2	4	-	6
2–3	3	2	1	6
3–4	4	3	1	8
4–5	6	6	1	13
5–6	2	3	1	6
6–7	3	5	1	9
7–8	3	3	2	8
8–9	3	4	-	7
9–10	1	3	-	4
10–11	9	1	-	10
11–12	1	1	-	2
Total	37	36	8	81

PD: Probable dengue, D+WS: Dengue with warning signs, SD: Severe dengue

patients of dengue is depicted in Table 1. Amongst these, 53 patients were male children and rest patients 28 were female. Thirty-three patients were rural and forty-eight were urban. Derangement of liver function is depicted in Table 2.

## DISCUSSION

In the present study, we measured the liver enzymes serum glutamate-pyruvate transaminase (SGPT), serum glutamic-oxaloacetic transaminase (SGOT), GGT, and ALP from day 1 then every alternate day till the day of discharge. It was found that excluding ALP which was raised only occasionally all the other three enzymes were raised throughout the whole period of dengue fever. The peak of the rise on an average was on day 5 of illness.

Fernando *et al.* from Sri Lanka found that all the patients with severe dengue had some degree of liver involvement while almost 85% of all patient with non-severe dengue had also some raised hepatic enzymes.<sup>[6]</sup> It is already established that raised levels of SGPT and SGOT are deemed as sine qua non of hepatic cell injury as these enzymes profusely poured into general circulation following a liver cell injury.

Out of these two SGPT though also present in skeletal muscle, brain, and intestine but in very low concentration and its rise is considered to be highly specific for liver cell injury only, on the other hand, rise of SGOT is seen not only in liver disorder but also in cardiac muscles, skeletal muscle injuries and is only a good supportive indicator of hepatic injury.<sup>[7]</sup> In their study, the elevation of SGOT was more pronounced than that of SGPT in severe damage suggesting that in severe dengue patient there is not only damage to liver cells but also concomitant injury to cardiac and or skeletal muscle. Our study also suggests that, since we did not perform the estimation of other most specific cardiac biomarkers; creatine phosphokinase-MB and cardiac troponin T and I and neither did we do skeletal muscle-specific enzymes; creatine kinase and serum aldose, we cannot conclude with surety that concomitant damage of cardiac and skeletal muscle occur also in severe dengue.

However, the presence of severe myalgia in dengue suggests all associated skeletal muscle damage but lack of

any cardiac symptoms apparently rules out possible cardiac muscle damage in severe dengue. However, a more detail cardiac studies should be done to rule out any possibility of cardiac involvement particularly in severe dengue cases. Some of patients particularly severe dengue had rise in serum bilirubin with pronounced rise in conjugated bilirubin suggesting a frank hepatocellular jaundice. Serum albumin also is reduced in only a few cases of severe dengue suggesting that the synthetic function of liver is the last item among the various liver function to be disrupted in dengue fever. Clinically, hyperbilirubinemia (more than two milligram per deciliter) with frank jaundice is also seldom seen in dengue fever except severe dengue where it is fairly common.

In our study, we had a mild rise in GGT and practically no rise in ALP. Both of these are signs of cholestasis in liver disorder but rise in ALP is a much better marker and most specific for cholestasis whereas it is not that specific. The latter is also raised in acute oxidative stress. Hence, the non rise of ALP and mild rise of GGT suggest that there is not much cholestasis in dengue liver derangement but there is definitely some acute oxidative stress. Acute oxidative stress causes reduction in cellular glutathione level with subsequent rise in GGT.<sup>[8,9]</sup> Hence, a rise of GGT in our study could be attributed to an acute oxidative stress. However, we should have measured serum 8 hydroxydeoxyguanosine levels to understand the levels of DNA damage to hepatocytes and other cells due to oxidative stress in dengue.

Narasimhan *et al.* also found hepatic involvement in dengue fever and noted that spectrum of liver disorder in dengue ranges from mild and asymptomatic biochemical derangement to severe jaundice and even total hepatic failure.<sup>[10]</sup> Low albumin levels are marker of clinical phase of the disease. Larreal *et al.* reported jaundice in two out of 63 cases of dengue fever.<sup>[11]</sup> Soni *et al.* also found liver disorder in dengue and like in our study they also noted higher SGOT than SGPT.<sup>[12]</sup> In a study from Pakistan found more than 3% of patients of dengue had hyperbilirubinemia comparable to our study which shows about 5% of such cases.<sup>[13]</sup>

**Table 2: Derangement of liver function in dengue patients**

Parameters	Day 1 on admission	Day 3 on admission	Day 5 on admission	Day 7 on admission	Day 9 on admission
Bilirubin mg/dl	1.8	2.1	2.66	2.31	1.84
SGOT IU/L	81	192	287	192	114
SGPT IU/L	69	177	254	157	98
GGT IU/L	58	96	126	102	82
Alk phosphatase IU/L	76	114	138	105	71
Albumin g/dl	4.2	4.1	4.3	4.2	4.1
Globulin g/dl	2.2	2.3	2.1	2.3	2.1
Platelet count Lacs/dl	0.86	0.79	0.76	0.84	1.1

SGPT: Serum glutamate-pyruvate transaminase, SGOT: Serum glutamic-oxaloacetic transaminase, GGT: Gamma-glutamyl transferase

Limitations of our study:

1. Done only in admitted children with dengue who are naturally more serious than those treated for dengue at home
2. Prothrombin time was not estimated in these dengue patients
3. Degree of oxidative stress was not measured.

Strength of power study:

Done in children infected with dengue whereas, very few studies have been done on children.

## CONCLUSION

In short, it can be concluded that within the limits of our study background in admitted children there is definitely damage of the liver in almost all cases of dengue. More the severity of dengue more is the height of hepatic damage.

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