

## Research Article

# Effect of dengue fever on serum aminotransferases in children

Rohit Khandelwal<sup>1\*</sup>, Leeni Mehta Khandelwal<sup>2</sup>, Susheela C.<sup>1</sup>

<sup>1</sup>Department of Paediatrics, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, Karnataka, India

<sup>2</sup>Department of Internal Medicine, Apollo Clinic and Hospital, Bangalore, Karnataka, India

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**\*Correspondence:**

Dr. Rohit Khandelwal,

E-mail: docrl09@gmail.com

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### ABSTRACT

**Background:** Dengue infection is associated with liver dysfunction, which tends to become severe with severe dengue. In the acute phase of the disease, an increase occurs in aminotransferases, the levels of which subsequently decrease as the liver function recovers. Significant rise of liver enzymes helps in recognition of severe forms of dengue infection.

**Methods:** The study was conducted in the Department of Pediatrics of Vydehi Institute of Medical Sciences and Research Center, Bangalore from January 2015 to June 2015. 50 patients of 1-14 years age group, who presented with fever of recent duration and serologically positive for dengue, were included in the study.

**Results:** 38% (19) were females and 62% (31) were males. NS1 was positive in 48% (24) and IgM was positive in 52% (26) of patients. IgG was negative in all the patients. AST was raised in 36% (18) of patients, ALT was raised in 34% (17) patients and ALP raised in 42% (21) patients. AST (Mean  $\pm$  SD 53.84 $\pm$ 43.32) was raised more than ALT (Mean  $\pm$  SD 48.76 $\pm$ 41.11)

**Conclusions:** Liver enzymes were mildly elevated in patients with dengue fever in the initial stage of illness. AST was elevated more than ALT.

**Keywords:** Dengue fever, Aminotransferases, ALT, AST, Severity

### INTRODUCTION

The term dengue fever came into general use only after 1828. Dengue viruses (DV) belong to family *Flaviviridae* and there are four serotypes of the virus referred to as DV-1, DV-2, DV-3 and DV-4. DV is a positive-stranded encapsulated RNA virus and is composed of three structural protein genes, which encode the nucleocapsid or core (C) protein, a membrane-associated (M) protein, an enveloped (E) glycoprotein and seven non-structural (NS) proteins. It is transmitted mainly by *Aedes aegypti* mosquito and also by *Aedes albopictus*. All four serotypes can cause the full spectrum of disease from a subclinical infection to a mild self-limiting disease, the dengue fever (DF) and a severe disease that may be fatal, the dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS).<sup>1</sup>

Dengue is endemic in 35 states/UTs. During 2012, 50222 cases and 242 deaths and during 2013, 75808 cases and 193 deaths were reported. During 2014 (till November), 33320 cases and 86 deaths have been reported.<sup>2</sup>

In dengue illness, varying degree of liver dysfunction is observed; severe dysfunction is more associated with severe dengue. Significant rise of liver enzymes helps in recognition of severe forms of dengue infection.<sup>3</sup> Aspartate transaminase (AST) and Alanine transaminase (ALT) are liver enzymes (aminotransferases) involved in amino acid metabolism. The inflammatory process resulting from infection by the dengue virus leads to a parenchymatous lesion that releases these markers into the blood. In the acute phase of the disease, an increase occurs in aminotransferases, the levels of which subsequently decrease as the liver recovers. Liver injury is nearly universal in adult patients with Dengue Infection

(DI). Little has been done to find out effect on liver. Hence the study has been carried out to study the effect of dengue on liver. Though liver involvement is asymptomatic in a large majority, in some patients it leads to clinical manifestations of liver disease and may occasionally lead to acute liver failure and death. Care must be taken to not make a mistaken diagnosis of viral hepatitis.<sup>4</sup> In a Taiwanese study, it was concluded that elevated aminotransferases along with others were useful predictive markers for early diagnosis of dengue infection.<sup>5</sup>

Liver enzymes were markedly elevated in more than 60% of the children who were dengue seropositive. Aspartate aminotransferase (AST) was elevated in a larger proportion of the patients. There was no significant difference between the subgroups of dengue with respect to liver function tests.<sup>6</sup>

The aim of the study was to evaluate the effect of dengue on liver aminotransferases in children.

**METHODS**

The study was conducted in the Department of Pediatrics of Vydehi Institute of Medical Sciences and Research Center, Bangalore from January 2015 to June 2015. A detailed history and a thorough clinical examination were done in all the cases. Data was collected in a prewritten proforma. Patients of 1-14 years age group, who presented with fever of recent duration, were included in the study. Other diseases like Malaria, enteric fever; Hepatitis A and Hepatitis B were excluded by history, examination and investigations.

80 patients with acute onset (1-5 days) of fever were included. Dengue was suspected in 55 children, who had two or more of the following symptoms: fever, pain abdomen, headache, myalgias, arthralgias, skin rash, nausea, vomiting, retroorbital pain, prostration and haemorrhagic manifestations. Out of these, 55 children, 50 who presented in early febrile period (1-5 days) and who were serologically positive for dengue irrespective of the presence or absence of haemorrhagic manifestations took part in the study. Tests for serum aminotransferase (AST, ALT) levels were performed for them and data was analysed statistically.

**Statistical methods**

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1,

Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

**Significant figures**

- + Suggestive significance (P value: 0.05<P<0.10)
- \* Moderately significant (P value: 0.01<P ≤ 0.05)
- \*\* Strongly significant (P value: P≤0.01)

**RESULTS**

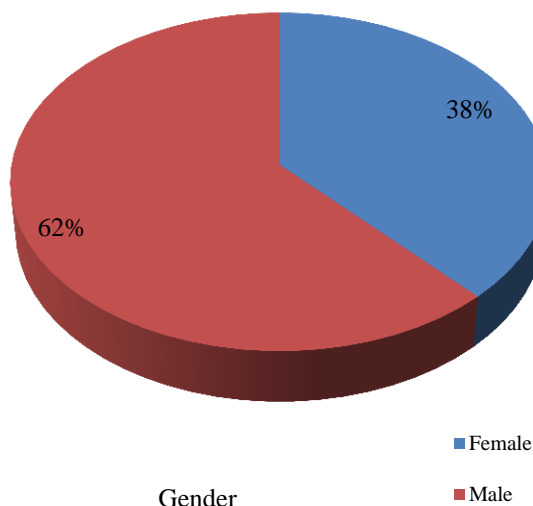
The study was an observational study and included 50 patients serologically positive for dengue fever of recent onset. Age group of 1-14 years was included. 20% belonged to 1-6 years group, 48% (7-12 years), 32% (>12 years) (Table 1, Figure 1).

**Table 1: Age distribution of patients studied.**

Age in years	No. of patients	%
1-6	10	20.0
7-12	24	48.0
>12	16	32.0
Total	50	100.0

Mean ± SD: 9.90±3.93

Out of these 38% were females and 62% were males.



**Figure 1: Age distribution of patients studied.**

NS1 was positive in 48% and IgM was positive in 52% of patients. IgG was negative in all the patients. In our study AST was raised in 36% of patients, ALT was raised in 34% patients and ALP raised in 42% patients. AST (Mean ± SD 53.84±43.32) was raised more than ALT (Mean ± SD 48.76±41.11) (Table 2).

**Table 2: Liver function test of patients studied.**

	No. of patients (n=50)	%	Mean ± SD
<b>Aspartate transaminases</b>			
<15	0	0.0	
15-50	32	64.0	53.84±43.32
>50	18	36.0	
<b>Alanine transaminases</b>			
<10	0	0.0	
10-35	33	66.0	48.76±41.11
>35	17	34.0	
<b>Alkaline phosphatase</b>			
<71	1	2.0	
71-142	28	56.0	131.40±41.48
>142	21	42.0	

**DISCUSSION**

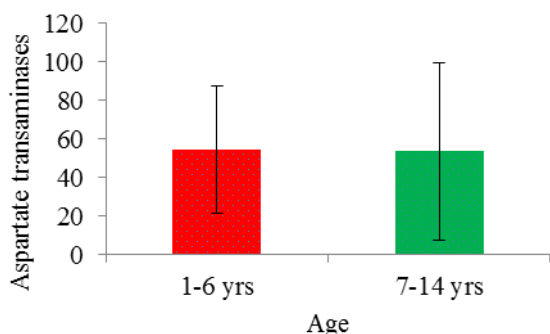
In our study of the total of 50 patients, 19 patients (38%) were female and 31 (62%) were male (range 1-14 years).

In our study AST was raised in 36% of patients, ALT was raised in 34% patients and ALP raised in 42 % patients. AST (Mean ± SD 53.84±43.32), (p = 0.958) was raised more than ALT (Mean ± SD 48.76±41.11), (p = 0.313) with insignificant p value.

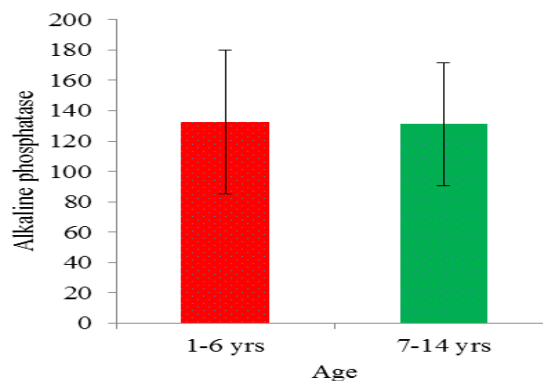
In a study group by Kalenahalli et al which included 110 children aged between 2-mo-14 years satisfying the WHO criteria for dengue fever, it was observed that ALT was elevated in 69.4% of DF, and raised AST in 88% of DF.<sup>7</sup> The rise was less significant in dengue fever without complications.

**Table 3: Comparison of liver function tests according to age in patients studied.**

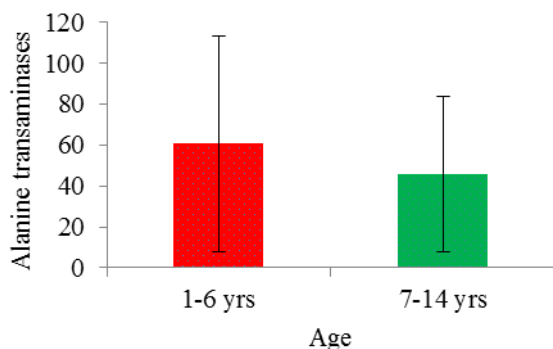
Variables	Age in years		Total	P value
	1-6 yrs	7-14 yrs		
Aspartate transaminases	54.50±32.79	53.68±45.92	53.84±43.32	0.958
Alanine transaminases	60.60±52.83	45.80±37.88	48.76±41.11	0.313
Alkaline phosphatase	132.50±47.24	131.13±40.57	131.40±41.48	0.926



**Figure 2A: Comparison of liver function tests according to age in patients; aspartate transaminases.**



**Figure 2C: Comparison of liver function tests according to age in patients; alkaline phosphatase.**



**Figure 2B: Comparison of liver function tests according to age in patients; alanine transaminases.**

In another study done in Vietnam, 644 dengue patients, of age greater than 14 years were included. In these patients AST and ALT levels began to increase slightly in the early febrile period: median (90% range) of 43 IU/L (18–314 IU/L) for AST levels and 40 IU/L (14–236 IU/L) for ALT levels. Both enzyme levels increased significantly in the critical period to 107 IU/L (30–483 IU/L) for AST and 83 IU/L (22–422 IU/L) for ALT, and reached peak concentrations of 138 IU/L (45–547 IU/L) for AST and 136 IU/L (31–574 IU/L) for ALT during the convalescent period.<sup>8</sup>

AST raise more than ALT in dengue may be due to involvement of myocytes. This differs from the pattern seen in viral hepatitis, in which ALT levels are usually higher than or equal to AST levels. It was observed that ALT was elevated in 69.6% cases of dengue fever.<sup>9</sup> Liver enzymes were markedly elevated in more than 60% of the children who were dengue seropositive. Aspartate aminotransferase (AST) was elevated in a larger proportion of the patients. There was no significant difference between the subgroups of dengue with respect to liver function tests.<sup>6</sup> Serum alanine and aspartate aminotransferase activities were elevated in 43 patients (96%) each; 5-fold elevated levels were more frequent in severe disease.<sup>10</sup>

In another study total of 336 patients receiving care at the Dengue Referral Center for Diagnosis and Treatment were included in this study between May and July 2003. Of these, 97 patients (57.4%) were female and 72 (42.6%) were male. Mean age of patients was 34.5 years (range 7-78 years). Out of 336 patients of the 169 serologically confirmed cases of dengue at the dengue referral center in Campos dos Goytacazes in the state of Rio de Janeiro, Brazil, In the cases classified as classic dengue, aminotransferases were high in 61.4%, while in cases of DHF, aminotransferases were abnormal in 76.2% of cases.<sup>4</sup> In a study, 240 Children with serologically positive dengue fever aged between 1 year to 18 years screened and included. Out of 240 children abnormal liver function tests were observed in dengue fever with warning signs and severe dengue. Severity of hepatic dysfunction noticed more in severe dengue cases. More than 10 fold increase in the levels of both ALT and AST were observed AST was elevated in 110(84.8%) dengue cases, ALT was elevated in 90(69.6%) cases of dengue fever.<sup>3</sup>

In a study in Taiwan, among 376 dengue seropositive patients, there were elevated serum levels of aminotransferase (AST,  $166 \pm 208$  U/L; ALT,  $82 \pm 103$  U/L.<sup>5</sup>

## CONCLUSION

Liver enzymes were mildly elevated in patients with dengue fever in the initial stage of illness. AST was elevated more than ALT. In this study patients with

dengue fever without complications were taken so it is concluded that uncomplicated dengue fever is associated lesser with derangement of liver enzymes.

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*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Gupta N, Srivastava S, Chaturvedi UA. Dengue in India. Indian J Med Res. 2012;9(136):373-90.
2. National vector borne disease control programme annual report 2014-15. Available from: <http://nvbdcp.gov.in/doc/annual-report-nvbdcp-2014-15.pdf>. Accessed February 5, 2016.
3. Surendra HS, Adarsh E, Hema D, Varshini P, Sirajudheen P. Study of liver profile in dengue fever. International journal of medical and applied sciences. 2015;4(3):153-8.
4. Desouza LJ, Nogueira RMR, Soars LC, Soares CEC, Ribas BF, Alves FP. The impact of dengue on liver function as evaluated by aminotransferase levels. Braz J Infect Dis. 2007;11(4):407-10.
5. Ho TS, Wang SM, Lin YS, Liu CC. Clinical and laboratory predictive markers for acute dengue infection. J biomed sci. 2013;10:75.
6. Narayanan M, Aravind MA, Thilothammal N, Prema R, Sargunam CR. Dengue fever epidemic in chennai - a study of clinical profile and outcome. Indian pediatrics. 2002;39:1027-33.
7. Jagadishkumar K, Jain P, Manjunath VG, Umesh L. Epatic involvement in dengue fever in children Iran j pediatr. 2012;22(2): 231-6.
8. Trung DT, Thao LTT, Hien TT, Hung NT. Liver involvement associated with dengue infection in adults in Vietnam. Am j trop med hyg. 2010;83(4):774-80.
9. Kamath SR, Ranjith S. Clinical features, complications and atypical manifestations of children with severe forms of dengue hemorrhagic fever in south India. Indian j pediatr. 2006;73(10):889-95.
10. Itha S, Kashyap R, Krishnani N, Vivek A, Saraswat VA, Choudhuri G, et al. Profile of liver involvement in dengue virus infection. Natl Med J India. 2005;18(3):127-30.

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