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## Study Of Liver Function Tests In Dengue Fever Patients / Biochemical Impact Of Dengue Virus On Liver Function Tests.

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### ABSTRACT

Dengue infection a major health problem worldwide including our country is the most prevalent arthropod borne viral illness in humans caused by dengue virus. Dengue has diverse clinical and biochemical presentations that effect the liver, the present study was conducted to assess the biochemical impact of dengue virus on liver function tests. A total of 100 dengue patients confirmed by serology were included in the study. All the patients were subjected to complete history taking and detailed parameters for liver function tests were done for all patients. A total of 100 dengue serology positive patient were included in the study. Among them there were 45% males and 55% females. In our study 98 patients had elevated serum AST levels with mean value of  $182.21 \pm 51.53$ U/L and the mean ALT levels were  $134.88 \pm 43.16$  IU/L. The level of AST are significantly higher when compared to ALT in most of the patients. This study highlights that estimating the levels of serum transaminases in dengue fever may help out in early detection of liver cell damage. Early alterations of these biochemical markers can predict the severity of liver damage due to dengue fever.

**Keywords:** Dengue virus DENV, Dengue fever - DF, Alanine aminotransferase – ALT, Aspartate aminotransferase – AST.

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## INTRODUCTION

Dengue virus (DENV) is most widespread arboviral disease transmitted to humans by bite of a female Aedes mosquito. This virus has 4 distinct serotypes (DENV 1–4) that cause a common febrile illness, called as dengue fever (DF), hence presents an enormous challenge to health in developing countries like India. Epidemic dengue is a major public health problem in South East Asia, especially in India where there is a reported case fatality ratio of 3–5%. [1] Outbreaks of dengue infection can be seen year after year especially during the monsoon season. Typical pattern of dengue fever has an incubation period of 4–8 days which is followed by onset of fever, generalized body ache, myalgia, arthralgia, and headache. [2] In the last few years, the classical presentation of dengue fever has expanded its horizon by involving various organ systems. [3] Four types of disease are seen - an asymptomatic stage, febrile stage, classical Dengue fever, Dengue hemorrhagic fever (DHF) including Dengue shock syndrome (DSS).

Dengue viral disease has been recognized as one of the most significant emerging global health problem in terms of morbidity and mortality as well as economic cost in tropical and subtropical areas. [4] The present study was conducted to assess the biochemical impact of dengue virus on liver function tests as in most patients of the dengue fever, hepatic involvement prolongs the clinical course of self-limiting viral infection and the spectrum of involvement include asymptomatic elevation of serum aminotransferase to occurrence of severe manifestation in the form of liver failure. [5]

## METHODS

This observational study was conducted at a tertiary care hospital in Maharashtra. A total of 100 dengue patients confirmed by serology were included in the study. These patients were confirmed by NS1 antigen and/or IgM dengue antibody done by Dengue IgG/IgM Quanticard and ELISA manufactured by J. Mitra and Co. Pvt. Ltd., New Delhi, India. All patients included were evaluated with detailed history including age, sex, presenting symptoms; history of co morbid illness. Under all aseptic precautions about 5ml of fasting morning blood samples were collected from antecubital vein in a plain vial without applying tourniquet. The blood was allowed to clot and was centrifuged at 1500 RPM for 10 minutes and serum was separated, and analyzed immediately on the same day for liver function tests. In case the sample analysis was delayed, it was refrigerated at 2-8°C for a maximum period of 3 days. The serum AST also called as serum glutamic oxaloacetic transaminases (SGOT) and ALT also called as serum glutamic pyruvic transaminase (SGPT) were estimated by enzymatic (kinetic) methods, analyzed by auto-analyzer – Siemens Dimension EXL 200, estimated by IFCC (International Federation of Clinical Chemistry) without pyridoxal phosphate activation. Total bilirubin, total protein, albumin and ALP were estimated by colorimetric assay. Patients with history of alcohol abuse, chronic liver disease, malaria, tuberculosis and history of intake of hepatotoxic drugs were excluded.

### Data Analysis

The data entry was carried using Microsoft Office Excel worksheet and then exported to statistical software and analyzed using appropriate statistical tests by using Statistical Package for Social Services (SPSS version 21 for MAC IBM, Inc.). The data obtained was compiled and analysed. p value of less than 0.05 was considered to be statistically significant.

### Ethical considerations

Approval was obtained from the subjects by taking the informed consent. The approval was on the agreement that patient anonymity must be maintained, good laboratory practice, quality control ensured, and that every finding would be treated with utmost confidentiality and for the purpose of this research only. All work was performed according to the International Guidelines for Human Experimentation in Biomedical Research [6].

## RESULTS

One hundred patients with serologically positive dengue were enrolled for the present study. Of 100 cases, 45 (45%) were male and 55 (55%) were female, Fig 1. The mean age of patients was  $35 \pm 11.4$  years. Maximum number of patients were seen in the age group of 21-30 years and 31-40 years i.e (35%) and

(25%) respectively [Table 1]. Results of hepatic dysfunction, in the form of raised total bilirubin values was present in 31% (31/100), raised direct bilirubin in 61% (61/100), decreased total protein in 40% (40/100), hypoalbuminaemia in 44% (44/100), raised AST in 98% (98/100), raised ALT in 96% (96/100) and raised ALP in 64% (64/100) patients. AST levels were  $(182.21 \pm 51.53\text{U/L})$  significantly higher than ALT levels  $(134.88 \pm 43.16)$  and ALP levels  $(124.38 \pm 66.6)$ ,  $p$  value  $< 0.0001$ . The details of biochemical parameters of patients are shown in Table 3.

**Table 1: Descriptive analysis of age in dengue patients (N = 100)**

Age Group	Percentage %
21-30	35%
31-40	25%
41-50	16%
51-60	15%
61-70	6%
>70	3%

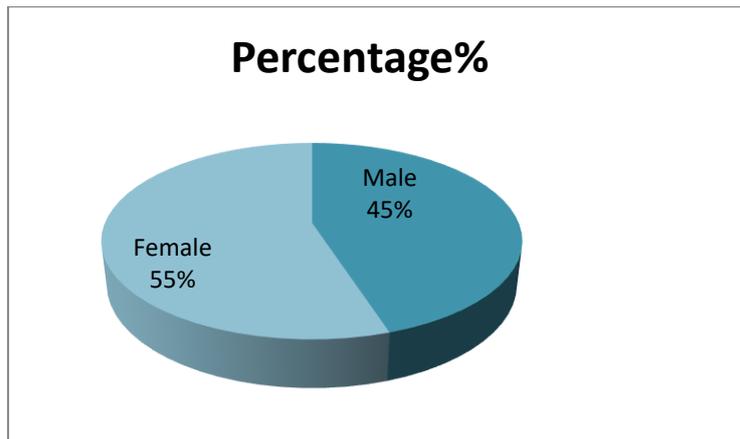
**Table 2: Descriptive analysis of gender in dengue patients (N=100)**

Gender	Number	Percentage (%)
Male	45	45%
female	55	55%

**Table 3: Descriptive Analysis of Liver Function Tests:**

Parameters	Number of Patients N= 100	Mean $\pm$ SD
<b>Total Bilirubin</b>		
▪ 0.3- 1.3	▪ 69	1.31 $\pm$ 0.78
▪ > 1.3	▪ 31	
<b>Direct Bilirubin</b>		
▪ 0.1- 0.4	▪ 39	0.70 $\pm$ 0.27
▪ > 0.4	▪ 61	
<b>Total Protein</b>		
▪ < 6.7	▪ 40	6.40 $\pm$ 1.50
▪ 6.7- 8.6	▪ 60	
<b>Serum Albumin</b>		
▪ < 3.5	▪ 36	3.48 $\pm$ 0.64
▪ > 3.5	▪ 44	
<b>AST/ SGOT (U/L)</b>		
▪ 12-38	▪ 02	182.21 $\pm$ 51.53
▪ >38	▪ 98	
<b>ALT/ SGPT (U/L)</b>		
▪ 7-41	▪ 04	134.88 $\pm$ 43.16
▪ > 41	▪ 96	
<b>ALP (U/L)</b>		
▪ 33- 96	▪ 36	124.38 $\pm$ 66.6
▪ > 96	▪ 64	

**Fig 1: Pie chart of gender distribution in dengue patients (N=100)**



**DISCUSSION**

In the present study, we evaluated the pattern of liver function parameters in one hundred serologically verified cases of dengue IgM infection. Infectious diseases such as dengue are being more and more recognized as an etiological agent of liver dysfunction. There was presence of hepatic dysfunction in most of our patients as evidenced by increased level of serum transaminases in patients, this collaborates with the the study conducted by Srivenu Itha et al where 97% had hepatic involvement with raised liver enzymes. Another study by Rajni R. shivkar et al showed that transaminase levels increase in almost all dengue patients.[7,8]

In our study, aspartate aminotransferase (AST) levels ( $182.21 \pm 51.53$  U/L) tend to be greater than alanine aminotransferase (ALT) levels ( $134.88 \pm 43$  U/L), which is in accordance with the results of other studies which state that aspartate aminotransferase (AST) levels in dengue infection tend to be greater than alanine aminotransferase (ALT) levels [9,10]. This pattern is similar to that we see in alcoholic hepatitis but differs from that seen in other viral hepatitis. The exact cause of this is uncertain, but it has been suggested that it may be due to excess release of AST from damaged myocytes during dengue infection.[11] This preferential elevation of liver enzymes, with AST being significantly higher than ALT was also noted in study done by Rajoo et al and this abnormality may act as an early indicator of dengue infection.[12]

Biochemical liver dysfunction, in the form of increased transaminases, was found in most of the patients in our study 96% - 98%, similar to the results of Rajoo et al (93.9%–97.7%) and other studies.[12,13,14] However, in a study by Souza et al AST and ALT were deranged only in 63.4% and 45% patients respectively.[9] Raised levels of ALP and serum bilirubin were noted in a smaller proportion of patients, as with the results of Rajoo et al and Itha et al. None of the patients had previous liver illness or abnormal AST and ALT levels, which support the association between developments of dengue fever and early alteration of the serum transaminases.

**CONCLUSION**

Dengue has numerous biochemical and clinical manifestations affecting the liver. Changes in serum transaminase levels pose a big challenge to the clinicians treating the condition.

The physicians treating the disease have a great difficulty in adjusting their serum transaminase levels. This study illustrates a potential contribution to the early detection of liver cell damage by measuring the rate of serum transaminasis in dengue fever. Early changes in biochemical markers such as Aspartate aminotransferase and Alanine aminotransferase can predict the severity of hepatic damage caused by dengue fever.

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