



## TO STUDY THAT: IS THERE ANY CORRELATION OF SEVERITY OF DENGUE FEVER WITH LEVELS OF AMINOTRANSFERASES?

### General Medicine

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### ABSTRACT

**INTRODUCTION:** Dengue fever (DF) is usually a self-limited mosquito borne viral disease. It is caused by one among the 4 subtypes of dengue viruses. Dengue fever is an arboviral infection transmitted by *Aedes aegypti* as well as *Aedes Albopictus*. Dengue viral infection has been recognized as one of the world's biggest emerging epidemic. Liver dysfunction in dengue is due to direct effects of the virus on liver cells and an adverse effect of host immune reaction against the virus. It has been shown that most patients with dengue fever have liver involvement in the form of elevated serum aminotransferases. Hence, evaluation of liver function, particularly the aminotransferases, should be a routine in the management of patients with dengue fever. **AIMS & OBJECTIVES:** To assess, is there any correlation of severity of dengue fever with levels of aminotransferases? **MATERIAL & METHODS:** This is an observational, prospective study and was conducted on patients who are diagnosed to have dengue (serologically and clinically) positive admitted in ICU, and Medicine wards of General Hospital, Jam-Khambhalia & tests were carried out. **OBSERVATIONS & RESULTS:** In this study we observed that male comprised of 55% and female were 45% of total dengue patients. Mean AST was found to be in increasing trend with disease severity. Mean ALT level was increased in moderate dengue patients than mild and severe category. **DISCUSSION:** In our prospective, observational study, we categorised them into mild, moderate and severe category according to Indian national guidelines. Platelet count level was significantly associated with category of the disease but did not have any association with serum aminotransferase level. We observed serum aminotransferase were significantly elevated (AST>ALT) in dengue patients but having no significant correlation with the severity. So, level of serum aminotransferase cannot be used to predict the severity of disease. In our study there was significant correlation between platelet Count and the severity of dengue fever patients.

### KEYWORDS

#### INTRODUCTION

The worldwide spread of dengue has increased dramatically now-a-days to be endemic in 112 countries of South East Asia, Africa, South and North America and the Mediterranean regions. In tropical and subtropical regions nearly about 2.5 billion people are at risk for dengue fever[1]. Immunology of Dengue is characterised by an initial viremic phase (febrile) which corresponds to the first 3 days of illness. Followed by a critical immune phase spanning from 3rd to 6th day of illness. The phase of dengue beyond 6th day of illness is called recovery phase.[2] The incidence of hepatic dysfunction in dengue fever is high.[3,4,5,6,7,8] Elevation of the liver enzymes AST and ALT is common in acute dengue illness, occurring in 65–97% of dengue patients, peaking during the convalescent period of illness (days 7–10).[9,10,11,12] The serum glutamic oxaloacetic transaminases (SGOT-AST) and serum glutamic pyruvic transaminases (SGPT-ALT) were found to be increased 5-10 times in dengue fever due to liver parenchymal damage caused by the virus.[3,4,6] Liver dysfunction in dengue is due to direct effects of the virus on liver cells and an adverse effects of host immune reaction against the virus. Virus has been identified in liver tissue and dengue antigen identified within liver cells of affected individuals leading to kupffer cell hyperplasia. Apoptotic hepatocytes are found to be co-localised with dengue virus infected hepatocytes, suggesting that hepatocytes are the major site of dengue virus replication in the liver.[8] Hence, evaluation of liver function, particularly the aminotransferases, should be a routine in the management of patients with dengue fever. With this study, we have tried to find out is there any correlation with disease severity?

#### AIM & OBJECTIVES

**AIM:** To assess, is there any correlation of severity of dengue fever with levels of aminotransferases?

**Primary Objective:** To measure serum aminotransferase level in patients with dengue fever.

**Secondary Objective:** To correlate serum aminotransferase level with the severity of dengue fever.

#### MATERIALS & METHODS

This is an observational, prospective study and was conducted on patients who are diagnosed to have dengue (serologically and clinically) positive admitted in ICU, and Medicine wards of General Hospital, Jam-Khambhalia.

#### Study Duration:

All patients admitted in various wards between January 2019 to June 2020 (1.5 yrs) fulfilling inclusion and exclusion criteria of this study were taken in the study. Patients were subjected to clinical examination & relevant blood investigation were performed at the time of admission & the results were statistically analysed.

#### Inclusion Criteria:

- Patients aged >18 years
- All serologically (ELISA) positive patient.
- Patients with informed consent.

#### Exclusion Criteria:

Chronic liver disease, viral hepatitis (Hepatitis A, B and C), Malaria, scrub typhus, leptospirosis. Typhoid and history of alcohol abuse, use of chronic/acute hepatotoxic drugs.

#### Statistical Analysis:

Data was entered in MS Excel and analysed using statistical for social sciences (SPSS). Descriptive format & diagrammatic presentation was done using bar diagram or pie chart as required. For descriptive analysis we used Mean, Standard Deviation, Ratio and proportion with percentage. The quantitative data was analysed using Independent Student's T test, Pearson's correlation test, ANOVA test. P<0.05 was be considered as level of statistical significance.

#### OBSERVATIONS & RESULTS

In this study we observed that male comprised of 55% and female were 45% of total dengue patients. Maximum patients had aminotransferase level raised <3 times the normal value (40 IU). 7% of patients had >10 times raised ALT levels compared to 6% of patients having AST level >10 times.

**Table 1: Mean levels of AST and ALT with Grading of Dengue Patients**

Values	Mild	Moderate	Severe	Total	P value
Mean of AST	152.02	189.12	238.69	183.07	0.55 (NS)
StdDev of AST	254.83	303.31	382.40	297.47	
Mean of ALT	122.09	149.73	141.88	141.64	0.68 (NS)
StdDev of ALT	149.65	216.22	148.90	195.16	

Mean AST was found to be in increasing trend with disease severity. Mean ALT level was increased in moderate dengue patients than mild and severe category.

**Table 2: Level of ALT with Grading of Dengue patients**

ALT (IU/L)	Grading			TOTAL	
	Mild	Mod	Severe		
Normal (Upto 40)	17	45	6	68	0.68 (NS)
<3times (41-120)	20	44	3	67	
3-10times (121-400)	15	30	6	51	
>10times (>400)	2	11	1	14	
TOTAL	54	130	16	200	

Total 68 (34%) patients had normal levels of ALT whereas 7% of patients had ALT levels raised >10 times.

**Table 3: Platelet counts in Dengue patients**

Platelet count(in thousands)	Number of Dengue patients	Percentage
<20	21	10.5
21-40	15	7.5
41-150	56	28
>151	108	54
TOTAL	200	100

Number of patients having thrombocytopenia (150k) is 46% and patients with normal platelet counts were 54%.

**Table 4: Comparison of Platelet count with level of ALT**

Platelet Count (thousands)	ALT				TOTAL	
	Normal (Upto 40)	<3times (41-120)	3-10times (121-400)	>10times (>400)		
<20	9	5	7	0	21	0.40 (NS)
21-40	5	6	3	2	16	
41-150	23	16	10	6	55	
>151	31	40	31	6	108	

Above table shows platelet counts decreased with increase in ALT levels.

There were few patients who had raised ALT levels but had normal platelet counts.

**Table 5: Comparison of platelet count with grading of dengue patients**

Platelet count (in thousands)	Grading			TOTAL	P value
	Mild	Moderate	Severe		
<20	0	15	6	21	<0.001 (HS)
21-40	0	13	2	15	
41-150	1	50	5	56	
>150	53	52	3	108	
TOTAL	54	130	16	200	

As category of severity of dengue increased, platelet counts decreased significantly. There was significant relationship between platelet counts and severity of dengue ( $p < 0.001$ ).

**Table 6: Correlation of Bleeding with levels of Aminotransferase**

	Bleeding	Aminotransferase level				P Value
		Normal (Upto 40)	<3times (41-120)	3-10times (121-400)	>10times (>400)	
AST	Present	3	0	0	1	0.06 (NS)
	Absent	62	70	53	11	
	TOTAL	65	70	53	12	
ALT	Present	3	0	0	1	0.09 (NS)
	Absent	65	67	51	13	
	TOTAL	68	67	51	14	

Only 4 patients presented with bleeding tendencies in our study, of which 3 had normal aminotransferase levels whereas in 1 patient levels were >10 times.

## DISCUSSION

This study was conducted at General Hospital, Jam-Khambhaliya and written informed consent during the period from January 2019 to June 2020. This prospective observational study was conducted on 200 patients. Patients diagnosed as Dengu positive were included in the study. Their history was taken and examinations were performed with all relevant routine investigations.

In our study mean level of AST in patients (was  $183.07 \pm 297.47$  U/L and that of ALT was  $141.64 \pm 195.16$  U/L which when compared was

statistically non significant ( $p=0.09$ , NS). In a study by Verma AK et al[20] mean AST value was  $396 \pm 746$  IU/L and mean ALT was  $285 \pm 460$  IU/L. Similar findings were reported by Govindarajan et al[13] who showed mean AST  $259.45$  U/L and mean ALT  $199.75$  U/L. Louiz J de S et al[14] showed their average AST level was greater than that of ALT in both DF and DHF. They also found higher average AST and ALT value in DHF than DF which is similar to our findings. Chhina et al[15] compared between the degree of rise of ALT and AST. Significantly more percentage of patients had AST values >10 times elevated as compared with ALT ( $p < 0.0001$ ). The above findings were also almost similar with the findings of Kuo et al[16], where 270 dengue patients were evaluated and had raised AST and ALT in 93.2% and 82.2% cases respectively with greater elevation of ALT than ALT which returned to normal after 3 weeks. The mean ALT level of all the patients was  $201.4$  U/L in our study. This value was comparable to results obtained by Chhina et al[15] ( $218.6$  U/L) and Manohar et al ( $201.1$  U/L). Studies done by Kittittrakul et al[17] showed mean ALT levels of  $152$  U/L and  $121$  U/L, respectively, which were lower than the levels observed in our study. Gandhi and Shetty et al[18] in their study showed mean AST levels of  $390.7 \pm 730.60$  U/L and mean ALT levels of  $296.9 \pm 562.08$  U/L which is similar to the findings of our study. In our study mean values of AST with mild dengue fever was  $152.02$  U/L, that of moderate dengue fever was  $189.12$  U/L and of severe dengue fever was  $238.69$  U/L. Mean ALT values with mild dengue fever was  $122.09$  U/L, of moderate dengue fever was  $149.73$  U/L and that of severe dengue fever was  $141.88$  U/L[15]. Chhina et al[15] compared mean values of AST and ALT in groups and observed that the mean values of AST in DF(277), DHF(478), DSS(1234) and mean ALT in DF(174),

DHF(254), DSS(819) was significantly different from our study as they did not exclude the patients with hepatitis and patients with other liver pathology. Luiz José de Souza et al[19] in their study observed that mean AST level in Dengue classic fever was  $89.8$  and Dengue Haemorrhagic fever (DHF) was  $127.1$ . Whereas ALT was  $84.6$  in Classic fever and  $100.2$  in DHF. In a study by Verma et al[20] showed reference value of AST and ALT was  $40$  U/L. Patients with normal aminotransferase levels were assigned Grade A. Those with the level of at least one of the aminotransferases elevated but less than 3 times the reference range were assigned Grade B. Patients with the level of at least one of the aminotransferases more than 3 times the reference range but less than 10 times the reference value were graded as C, and those with an increase in the level of one or both the enzymes more than 10 times were classified as Grade D. Twelve patients had normal level of serum aminotransferase (grade A, 28.5%), 30 (71.4%) had elevated enzymes in which 17 falling into the grade B (40.4%), 10 in grade C (23.3%) and 3 in the group D (7.1%). Among 30 patients with raised serum aminotransferase all had elevated AST whereas only 24 (80%) had elevated ALT.

In our study we classified range of platelet counts between less than 20K, from 21k to 40k, 41k to 150k and more than 151k, and observed that patients were having platelet count less than 150k were 46%. Mukker P et al[12] studied 123 dengue patients and ranged their platelet counts into three groups which showed that 52 of them had platelet counts below 20,000, 69 patients had counts between 20,000 to 100000 and 3 patients had counts above 100000. Which is different from our study. It might be due to the fact that their study was conducted in ICU patients only. Pandey et al[18] observed 35% patients were having platelet count less than 10k, 34.2% patients were having platelet count less than 25k and 44.2% patients having platelet count less than 75k and 11.42% patients were having between 75k to 1.5 lakh which is different from our study as they only observed in patients having thrombocytopenia. Although above studies showed thrombocytopenia in more number of patients as compared to our study, but trend of decrease in platelet count was similar. The proposed mechanism of thrombocytopenia is down-regulation of haematopoiesis as it is a protective mechanism of the microenvironment that reduces the damage to the marrow stem/progenitor cell during the subsequent process of elimination of infected cells.[9] We compared platelet count with severity of dengue and observed that it was significantly correlated. Similarly Navya et al[22], studied the association between platelet parameters like platelet count, MPV and PDW and severity of the disease (DF/DHF/DSS). Major difference was seen between severity of the thrombocytopenia and severity of the disease (P value - 0.013). Dengue positive cases were associated with low MPV and high PDW values in 72% cases and 92% cases respectively. They found Low MPV which shows sensitivity for dengue fever and could be used as a significant marker for diagnosing dengue fever in endemic area.[9] Similarly Mukker P et al[61] observed that low platelet count, low PCT and high PDW may be used as predictor of severity of Dengue

infection.[23] Mean AST/ALT in dengue patient with increased haematocrit was 151.2/145.6 which is less than mean AST/ALT of all dengue patients included in our study (183/141.6) and having no significant correlation with it. In a similar study by Potluri VT et al[23] in their study they concluded that Dengue patients with increased haematocrit had mean AST/ALT (151.9/101.5) which is similar to our study showing no significant correlation.

We observed that number of patients having thrombocytopenia (<150k) was 46% and patients with normal platelet counts were 54% and having no significant association with serum aminotransferase level. [9]. In our study there was significant correlation between platelet count and severity of dengue patients. As thrombocytopenia was seen more in severe category. We observed serum aminotransferase were significantly elevated (AST>ALT) in dengue patients but having no significant correlation with the severity. So, level of serum aminotransferase cannot be used to predict the severity of disease.

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