ORIGINAL RESEARCH PAPER

General Medicine

LIVER TRANSAMINASES AND PLATELET COUNT CORRELATION IN DENGUE PATIENTS FROM TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Dengue is the arboviral febrile illness, which affects the vascular, muscular, and hematological systems. One of the standards used by WHO recommendations as a possible predictor of the clinical severity of infection is thrombocytopenia. A well-known aspect of dengue illness that is accompanied by hepatomegaly and elevated serum transaminase levels is hepatic dysfunction. **Objective:** This study's objective was to determine the liver's contribution to dengue infection during the severity of dengue infection by comparing platelet counts and liver transaminase enzyme levels in a tertiary care facility. **Method:** Admitted cases of Dengue fever (dengue serology positive –IgM) were divided into 3 groups: DF, DHF, DSS based on the clinical and laboratory finding and relation of aminotransferases level were analyzed. Elevation in LFTs were co-related with DF, DHF, DSS. Result: In DF there was 7% patients having mild platelets and 93% patients having moderate platelets. In DHF, 7.4% patients had mild platelets, 70.4% having moderate and 22.2% had severe platelets. In DSS 79.3% patients had moderate platelets and 20.7% had severe platelets. The association was found significant. **Conclusion:** Transaminase levels rise in nearly all dengue cases, according to our study's findings. Since AST and ALT levels are negatively correlated, an increase in dengue severity is accompanied by an increase in AST and ALT levels, and decrease in platelet count.

INTRODUCTION

Breakbone fever, often known as dengue, is a serious and widely spread mosquito-borne viral virus that causes feverish sickness in tropical and subtropical regions [1,2]. There are 4 different serotypes of a single-stranded RNA virus known as the dengue virus (DENV): DEN-1, DEN-2, DEN-3, and DEN-4[1]. The virus is spread through the Aedes aegypti mosquito's bite [1,3]. Dengue fever (DF), dengue haemorrhagic fever (DHF), and dengue shock syndrome are among the symptoms of dengue virus infection (DSS) [2,4,5]. Annual reports to the World Health Organization include between 2, 50,000 and 5, 00,000 cases of DHF and around 100 million cases of DF (WHO) [4].

The classic symptoms of dengue fever include fever, a strong myalgia, and a retro-orbital headache [5]. DHF and dengue shock syndrome (DSS) are two more severe illness forms of Dengue [5,6]. DHF is characterised by abnormal haemostasis and plasma leakage, which present clinically as thrombocytopenia, spontaneous bleeding, and haemoconcentration close to the time of defervescence, usually after 5 days of fever [4,5,7]. One of the standards utilised by WHO recommendations as a potential predictor of the clinical severity of infection is thrombocytopenia. The definition generally refers to rapid drop or a platelet count of fewer than 1,50,000 per microliter of blood in the most recent WHO recommendations [8]. The vascular, muscular, and haematological systems are all affected by dengue infection (9). A case of DHF with either tachycardia, a pulse pressure of 20 mmHg or lower, or a systolic blood pressure of 90 mmHg, is known as dengue shock syndrome [10].

Moreover, hepatic dysfunction, which is characterised by hepatomegaly and an increase in blood transaminase levels, is a well-known feature of dengue infection. This liver dysfunction may be caused by a direct viral impact on hepatocytes or by an improperly controlled host immunological response to an infection [2,9]. Transaminases are released into the blood during the inflammatory response to a parenchymatous lesion [12]. Some studies have found elevated levels of liver transaminase enzymes in dengue infected patients[2,5,9].

We chose to examine the involvement of the liver in serologically identified dengue patients by comparing liver transaminase levels with platelet counts throughout the critical phase (4-6 days of sickness), as this period is more likely to result in complications from the illness such as DHF or DSS [4,7].

In dengue patients during the crucial phase, platelet count is employed as a measure to correlate liver transaminase levels is one of the important criteria used by WHO to indicate severity of the dengue infection[10,11].

MATERIALS AND METHODS

This was a Prospective observational cross-sectional study which has been carried out Department of General Medicine at Tertiary care teaching institute, Mau, Atariya, Sitapur. Study Period was18 months from the commencement i.e., from February 2021 to July 2022. The current study focused on dengue patients with a serological diagnosis who were older than 18 years. Using a solid phase immunochromatographic test kit, anti-IgM antibodies or the presence of NS-1 antigen in the patient's serum were used to confirm the diagnosis of dengue. Patients were thought to be presently infected with the dengue virus if the test showed positive results for IgM or NS1 Antigen.

Exclusion Criteria
1. Patients with Chronic Liver Disease of any origin who have been previously identified or recently discovered (As evident by the clinico-radiologic and biochemical parameters).
2. Individuals with a known recent history of taking any hepatotoxic or comparable medicines that affect the way the liver works.
3. Individuals who suffer from Multiple Organ Dysfunction Syndrome (MODS) or sepsis-related decreased liver functioning (MODS) unrelated to Dengue infection.

Sample Size
Calculation Formula
Cochran's Formula:-
• sample size (n)

- $n = Z \propto * p * q/d^2$
- Where n = required sample size
- value of z at α =5% level of significance=1.96
- P=0.82, q=0.18 with precision of 0.06
- The calculated sample size 171

Study population was comprised of 171 serologically diagnosed dengue patient which were subcategorized into 3 groups on the basis of platelet count and based on severity of dengue disease i.e. dengue fever (DF), dengue haemorrhagic fever (DHF), and dengue shock syndrome (DSS) according to WHO criteria (2,4,5):-
1. In total of 171 patients, 86 (50.3%) had DF, 58 (33.9%) had DHF and 27 (15.8%) patients had DSS.
2. In the present study, 8 patients (4.7%) had platelet counts between 51,000 and 1 lakh (mild thrombocytopenia), 145 patients (84.8%) had platelet counts between 21,000 and 50,000 (moderate thrombocytopenia) while the remaining 18 patients (10.5%) had platelet counts <20,000 (severe thrombocytopenia).

METHOD
The study was undertaken in the Department of Medicine at Tertiary care teaching institute, Mau, Atariya, Sitapur, during the study period from February 2021 to July 2022.

Patients have their history taken according to a questionnaire and subjected to clinical examination and patients will be subjected to the investigations of complete blood count, blood urea, serum creatinine, RDT for MP, Widal, HBsAg, anti HCV, Chest X-ray, USG abdomen and liver function test.

All adult patients admitted with fever and thrombocytopenia during the study period who were fulfilling the inclusion criteria, were registered for the study after informed consent and ethical committee approval. Detailed proforma was filled with, age, sex, address, presenting complaints, clinical features, and examination findings. Lab investigations like CBC, AST, ALT levels at the time of admission Day (from day 2-6 of fever) were estimated.

Statistical Analysis
The data are reported as the mean +/- SD or the median, depending on their distribution. Frequencies are expressed in percentages. Comparison between groups was made by the Non parametric Mann - Whitney test. The chi square test and Fishers" exact test were used assess differences in categoric variables between groups. Binary Logistic regression was used to assess the variables & Odds ratio was performed. A p value of <0.05 using a two-tailed test was taken as being of significance for all statistical tests. All data were analysed with a statistical software package (SPSS, version 23.0 for windows)

RESULT
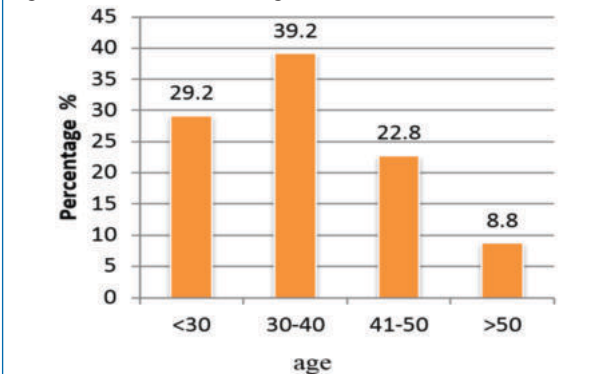1. Mean age was 36.31±10.96 and median was 38. Minimum age was 18 and maximum age was 82.

Fig 1: - Descriptive analysis of age (Mean age was 36.31±10.96 and median was 38)

2. The mean AST of patients was 186.99+154.03 and median was 168.0. the mean ALT/SGPT of patients was 135.48+117.56 and median was 105.0.

3. The frequency distribution of severity of dengue of patients. In total of 171 patients, 86 (50.3%) had DF, 58 (33.9%) had DHF and 27 (15.8%) patients had DSS.
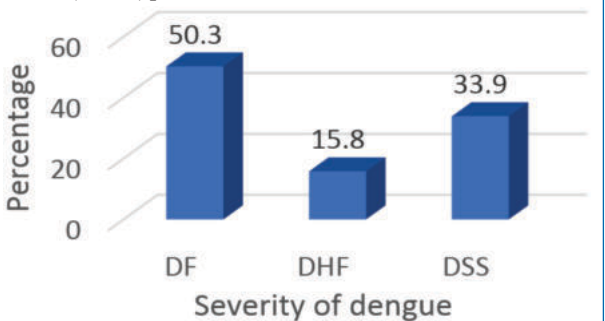

Fig 2: - Frequency distribution of severity of dengue

4. The mean AST (IU/L)/SGOT of DF, DHF and DSS patients was 78.73±93.28, 254.96±112.9, 315.88±123.26. There was a significant difference (<0.001 and 2 value = 100.74) found when they were associated

Table 1: Association of AST (IU/L)/SGOT with severity of dengue

	Severity of Dengue						χ2 values	P value
	DF		DHF		DSS			
	Mean	SD	Mean	SD	Mean	SD		
AST (IU/L)/SGOT	78.73	93.28	254.96	112.90	315.88	123.26	100.74	<0.001

5. The frequency distribution of AST. Out of all 171 patients, 14% had AST between 45 to <100, 16.4% had between 100 to <200, 17.5% had 200 to <300, 15.8% had 300 to <400, 10.5% patients had AST level more than 400; 25.7% had normal AST level.
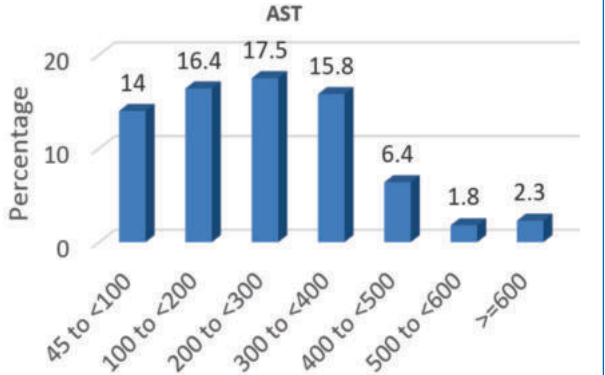

Fig. 3: - Frequency distribution of AST

6. The mean ALT (IU/L)/SGPT of DF, DHF and DSS patients was 49.97±54.77, 186.41±90.73, 238.57±99.59. There was a significant difference (<0.001 and 2 value = 104.13) found when they were associated.

Table 2: - Association of ALT with severity of dengue.

	Severity of Dengue						χ2 values	p value
	DF		DHF		DSS			
	Mean	SD	Mean	SD	Mean	SD		
ALT(IU/L)/SGPT	49.97	54.77	186.41	90.73	238.57	99.59	104.13	<0.001

7. The frequency distribution of ALT. Out of all 171 patients, 9.4% had ALT between 55 to <100, 23.4% had between 100 to <200, 18.7% had 200 to <300, 7% had 300 to <400, 1.8% patients had ALT level more than 400; 39.8% had normal ALT level.
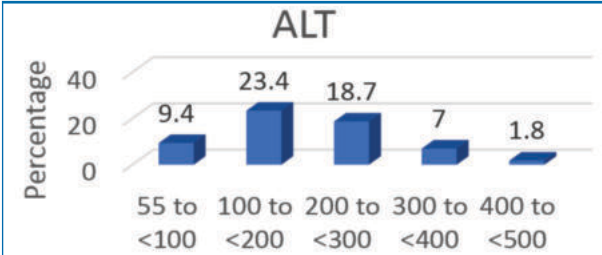
Fig. 4:- Frequency distribution of ALT

8.The mean platelets of patients were 70300+17798.15 and median was 70000.

9. The frequency distribution of platelets. In total of 171 patients, 145 (84.8%) had moderate platelets, 18 (10.5%) had severe and 8 (4.7%) patients had mild platelets.
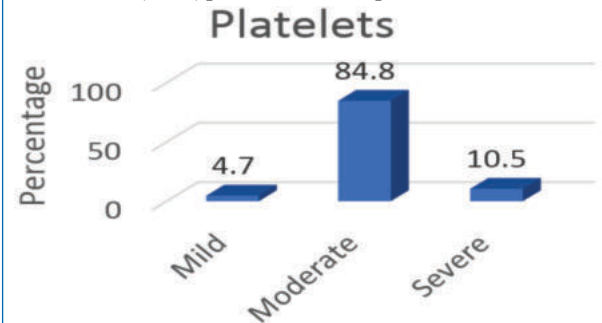

Fig. 5: Frequency distribution of platelets

10.The mean Platelets of DF, DHF and DSS patients was 79200±14064.65, 63700±18793.6, 60100±15545.54. There was a significant difference (<0.001 and χ2 value = 42.32) found when they were associated.

Table 3: Association of Platelets with severity of dengue.

	Severity of Dengue						χ2 values	p value
	DF		DHF		DSS			
	Mean	SD	Mean	SD	Mean	SD		
Platelets (mm3)	7920 0.00	1406 4.65	63700 .00	1879 3.60	6010 0.00	1554 5.54	42.32	<0.001

- 11. The association of Platelets with severity of dengue in the patients. In DF there was 7% patients having mild platelets and 93% patients having moderate platelets.
- In DHF, 7.4% patients had mild platelets, 70.4% having moderate and 22.2% had severe platelets.
- In DSS 79.3% patients had moderate platelets and 20.7% had severe platelets. The association was found significant.

Applied χ2 test for significance. χ2 values=23.92; df=4; p-value=<0.001; consider highly significant.

Table 4 & Fig. 6: - Association of platelets with severity of dengue
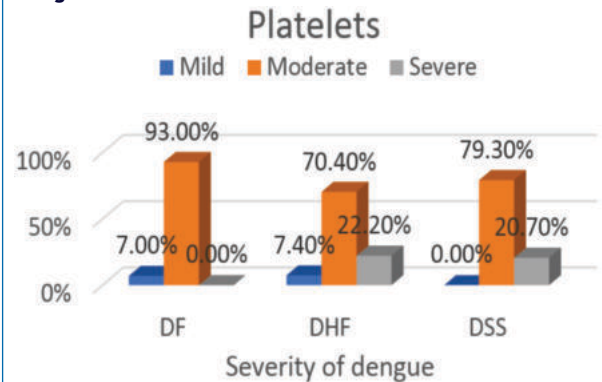
Platelets	Severity of Dengue					
	DF		DHF		DSS	
	N	%	N	%	N	%
Mild	6	7.0%	2	7.4%	0	.0%
Moderate	80	93.0%	19	70.4%	46	79.3%
Severe	0	.0%	6	22.2%	12	20.7%

12.The correlation of AST & ALT with Platelets. AST & ALT is found to be highly significant when co-related platelets r =-0.539 & r = - 0.548 respectively i.e., Negatively corelated.

Table 8: The correlation of AST & ALT with Platelets.

	AST	
	Spearman's rho Correlation coefficient(r)	p-value
Platelets (mm3)	-0.539	<0.001
	ALT	
	Spearman's rho Correlation coefficient(r)	p-value
Platelets (mm3)	-0.548	<0.001

DISCUSSION

Dengue is a significant arboviral disease with a wide range of symptoms, including silent fever, thrombocytopenia, abnormal haemostasis, i.e., DHF, and, in severe cases, circulatory compromise that can culminate in dengue shock syndrome, a potentially fatal condition (DSS)[1,2,3,4,5,6].

One of the criteria cited by WHO recommendations as a potential predictor of the clinical severity of dengue infection has always been thrombocytopenia[8]. Hepatic dysfunction is a common complication of dengue infection and may result from either the virus's direct impact on liver cells or from improperly controlled host immunological responses to the virus[9].

Increased levels of the liver transaminase enzyme can be used to biochemically identify liver involvement in dengue[2,4,9,12].

According to WHO standards from 1997 and 2009, platelet count, which is a measure of the severity of dengue infection, is correlated with liver transaminases in our study[10,11].

In the present study, total of 171 patients, 86 (50.3%) had DF, 58 (33.9%) had DHF and 27 (15.8%) patients had DSS.

The raised AST levels were found in 74.3% of patients, whereas raised ALT levels were found in 60.2% of patients. The mean AST of patients was 186.99+154.03 and median was 168.0. The mean ALT/SGPT of patients was 135.48+117.56 and median was 105.

Out of all 171 patients, 14% had AST between 45 to <100, 16.4% had between 100 to <200, 17.5% had 200 to <300, 15.8% had 300 to <400, 10.5% patients had AST level more than 400; 25.7% had normal AST level. Out of all 171 patients, 9.4% had ALT between 55 to <100, 23.4% had between 100 to <200, 18.7% had 200 to <300, 7% had 300 to <400, 1.8% patients had ALT level more than 400; 39.8% had normal ALT level.

Moreover, Kuo et al. Discovered abnormal AST and ALT levels in 93.3% and 82.2% of their research of 270 dengue patients[13].

Hence, irregularity in AST levels is greater than that in ALT, which is consistent with Wong and Shen's discovery[14]. This is also consistent with the results of the study by Nguyen et al., which revealed that AST values were commonly reported to be abnormal and occasionally reached values greater than those of ALT, approximately 97.7% and 37.3% over normal levels, respectively[15].

In the present study, 8 patients (4.7%) had platelet counts between 51,000 and 1 lakh (mild thrombocytopenia), 145

patients (84.8%) had platelet counts between 21,000 and 50,000 (moderate thrombocytopenia) while the remaining 18 patients (10.5%) had platelet counts <20,000 (severe thrombocytopenia). In our study, all cases with severe thrombocytopenia and greater percentage of patients with moderate thrombocytopenia presented with DHF/DSS when compared to those with mild thrombocytopenia. A significant drop in platelet counts was noted as the patient presented with symptoms of DHF/DSS. Among the cases with thrombocytopenia, it was noted that 25% of cases (2/8 patients) with mild thrombocytopenia, 44.8% of cases (65/145 patients) with moderate thrombocytopenia and 100% of cases (18/18 patients) with severe thrombocytopenia presented with DHF/DSS. A significant association was observed between the severity of thrombocytopenia and the clinical presentation of DHF/DSS (P<0.001). All cases with severe thrombocytopenia and greater percentage of patients with moderate thrombocytopenia presented with DHF/DSS when compared to those with mild thrombocytopenia. A significant drop in platelet counts was noted as the patient presented with symptoms of DHF/DSS.

The present study is supported by Mourao et al. who has observed that patients with DHF had lower platelet counts than patients with only DF[16].

In all dengue patients, regardless of platelet level, we found a negative association between AST and ALT with platelet count (r = -0.539 and r = -0.548), and this correlation was statistically significant (P value 0.001).(Table 8)

Our results corroborate those of Lee L.K., who investigated the clinical relevance of AST and ALT for DHF and severe dengue and came to the conclusion that aminotransferase levels rose with the severity of the disease. Also, they noted the highest AST and ALT values during the febrile and severe phases of dengue fever[17].

A negative link between AST and ALT levels and platelet count, supporting the hypothesis that an increase in dengue severity is associated with an increase in AST and ALT levels, which is shown by a decrease in platelet count. This shows that when dengue's platelet count declines, the likelihood of hepatic dysfunction—as measured by an increase in AST and ALT—increases.

Our results are in line with those of Dinh the Trung et al., who examined liver involvement brought on by dengue in adults in Vietnam and discovered that transaminase levels rose in almost all dengue patients and correlated with other indicators of disease severity, paying particular attention to the coagulation profile[2].

Furthermore, our results are in line with those of LA Villar-Centeno, who investigated biochemical changes in DHF and came to the conclusion that early changes in biochemical markers might be utilised to predict DHF in dengue fever patients[4].

CONCLUSION
Hence, we may say that several levels of hepatic dysfunction are caused by dengue, ranging from a moderate increase in AST and ALT to 10 times increase in AST and ALT in severe dengue infection. Hence, it is crucial to test and monitor AST and ALT levels in dengue-infected individuals because in our investigation, higher transaminase levels were linked to a decline in platelet count and, consequently, to the severity of the disease

Early detection and appropriate treatment of dengue patients enhance the prognosis and lessen co-morbidities. Hence, AST and ALT measurements can be used to assess the extent of liver damage caused by dengue infection since a lack of clotting factors, which are produced by the liver, might exacerbate the haemorrhagic state in DHF and DSS. We lacked information on dengue virus serotyping, nevertheless. Children were not included in the study; only the adult dengue patient group was examined. Results require confirmation in a sizable study population.

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