

Dengue Severity and Liver Enzymes: An Investigative Cross-Sectional Study

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Abstract:

Background and Objectives: This study at Geetanjali Medical College and Hospital, Udaipur, assessed Dengue severity and its association with liver enzyme levels in 153 Dengue-positive patients.

Materials and Methods: The study included 101 males and 52 females, with age groups 21-40 (DF), 41-60 (DHF), and 61-80 (DSS) most affected. Exclusion criteria included malaria, liver cirrhosis, viral hepatitis, and hepatotoxic drugs. Liver Enzymes were estimated using standard biochemical methods. Clinical profile of patients was recorded.

Results: Common complaints were fever, abdominal pain, rash, vomiting, headache, and joint pain. Bleeding occurred in 28.75% of cases. AST was elevated (> 40 U/L) in 91.5% of patients. DF had 87.3% raised AST (mean 154.17), while DHF and DSS had 100% elevation (mean 355.87 and 814.79, respectively). ALT was elevated (> 40 U/L) in 89.5% of patients. DF had 84.3% raised ALT (mean 91.7), while DHF and DSS had 100% elevation (mean 136.6 and 368.86, respectively).

Conclusion: This study reveals a significant link between elevated liver enzymes (AST and ALT) and Dengue severity. Higher elevations were seen in severe cases, suggesting potential as markers for Dengue prognosis and severity assessment.

Keywords: Dengue, Prognosis, Liver Enzymes, Hemorrhagic Fever.

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Introduction

Dengue infections, caused by four distinct dengue virus serotypes, are a significant global health concern. Dengue fever, characterized by symptoms such as fever and joint pain, has seen a fourfold increase in its global burden in recent decades, with approximately 2.5 billion people at risk of infection [1].

These infections can range from mild dengue fever to severe dengue, also known as dengue hemorrhagic fever (DHF), which can lead to capillary leakage, shock, organ dysfunction, and bleeding. Unfortunately, there are no specific antiviral medications or vaccines available for dengue, and treatment primarily focuses on fluid replacement in severe cases [2].

Severe dengue is marked by plasma leakage and impaired blood clotting, resulting in symptoms like increased hematocrit, reduced plasma proteins, pleural effusions, and ascites, all contributing to hypovolemic shock [3].

Dengue was previously classified into dengue fever and DHF but was reclassified by the World Health Organization (WHO) in 2009 to emphasize severity levels, categorizing patients as having dengue with or without warning signals or as having severe dengue based on clinical and laboratory data [4].

Dengue virus infects the liver, sometimes causing asymptomatic involvement but occasionally leading to acute fulminant hepatic failure. Hepatic impairment is a notable aspect of Dengue virus infection, affecting hepatocytes and Kupffer cells. Elevated liver enzyme levels, especially aspartate transaminase (AST) and alanine transaminase (ALT), are common in severe dengue, suggesting a link between enzyme levels and disease severity [5-8].

In conclusion, dengue infections have become a growing global concern, with a significant increase in cases and associated morbidity. Understanding

the relationship between liver enzymes and disease severity is crucial for early diagnosis and the management of severe cases.

Materials and Methods

This observational cross-sectional study was conducted over a duration of 18 months, spanning from June 2020 to November 2021, within the General Medicine ward and ICU at Geetanjali Medical College Hospital in Udaipur. The study aimed to assess the association between liver enzyme levels and the severity of Dengue infection. Inclusion criteria comprised Dengue-positive patients confirmed through ELISA tests for NS1 antigen and IgM/IgG antibodies, with an age criterion of over 18 years, regardless of gender. Exclusion criteria excluded patients with other diseases such as malaria, liver cirrhosis, enteric fever, and viral hepatitis, as well as those taking hepatotoxic drugs. A sample size of 153 consecutive patients meeting the study criteria was included during the study period.

Laboratory testing involved the use of NS1 early dengue ELISA for acute Dengue infection confirmation, as well as capture-IgM and IgG ELISA to differentiate between primary and secondary Dengue infections. Biochemical markers, including liver transaminases and serum albumin, were measured. Platelet count, white blood cell count, and hemoglobin levels were also assessed.

Operational definitions included.

Dengue infection diagnosis: Febrile illness with dengue-specific IgM capture antibody or NS1 antigen detection.

Dengue Hemorrhagic Fever (DHF): DF with hemorrhagic manifestations, low platelet count, and capillary leakage.

Dengue Shock Syndrome (DSS): Evidence of circulatory failure, pulse pressure ≤ 20 mmHg, hypotension, or shock.

DHF and DSS categorized as severe dengue infections.

Data collection was carried out using a pre-designed semi-structured study proforma, encompassing demographic, clinical, and laboratory data. Statistical analysis involved descriptive analysis, chi-square tests, and Student t-tests, conducted using SPSS software version 24.0.

Ethically, the research adhered to the Helsinki Declaration, securing prior approval from the Institutional Ethics Committee and obtaining written informed consent from all participants.

Results

In terms of age distribution, the majority of patients were male, constituting 66.01% of the total, while female patients comprised 33.99%. Further categorizing the age groups, it was observed that patients aged 20-40 years were the most prevalent, accounting for 38.56% of the total, followed by those aged 41-60 years (35.29%) and 61-80 years (18.30%). The least represented age group was those under 20 years, making up 7.84% of the study population (Table 1). Regarding the severity of the disease, the data revealed that Dengue Fever (DF) was the most common, with 66.67% of the patients falling into this category. Dengue Hemorrhagic Fever (DHF) was diagnosed in 24.18% of the cases, indicating a significant proportion of moderately severe cases. Dengue Shock Syndrome (DSS), the most severe form of the disease, was observed in 9.15% of the patients (Table 1).

Table 1: Demographic and Disease Severity Parameters

Parameter	n	%
Age		
Male	101	66.01
Female	52	33.99
Gender		
Less than 20 years	12	7.84
20-40 years	59	38.56
41-60 years	54	35.29
61-80 years	28	18.30
Severity of Disease		
Dengue Fever (DF)	102	66.67
Dengue Hemorrhagic Fever (DHF)	37	24.18
Dengue Shock Syndrome (DSS)	14	9.15

The most frequently reported symptom was Fever, followed by abdominal pain (Table 2).

Table 2: Presenting Clinical Symptoms in study population.

Presenting Symptoms	Frequency	Percent
Fever	76	49.67
Pain abdomen	70	45.75
Rash	62	40.52
Vomiting	60	39.22
Headache	54	35.29
Joint pain	51	33.33

Table 3 provides insight into the Relationship between Liver Enzymes and Dengue Severity. The levels of AST and ALT exhibited a notable increase in tandem with the severity of dengue.

Table 3: Association of Liver Enzymes with Dengue severity

Liver Enzymes	DF		DHF		DSS		p Value
	Mean	SD	Mean	SD	Mean	SD	
Aspartate Aminotransferase [AST] (U/L)	154.17	44.73	355.87	8.26	814.79	36.65	< 0.01
Alanine Aminotransferase [ALT] (U/L)	91.77	22.41	136.6	6.76	368.86	13.63	< 0.01
Alkaline Phosphatase [ALP] (U/L)	135.7	17.86	133.3	19.02	136.29	17.31	0.76

Discussion

In our investigation, we included a cohort of 153 patients who satisfied the specified study criteria. Among these participants, 101 individuals (66.01 percent) were male, while 52 individuals (33.98 percent) were female. Categorically, 102 patients (66.7 percent) were diagnosed with Dengue Fever (DF), 37 patients (24.2 percent) exhibited symptoms of Dengue Hemorrhagic Fever (DHF), and 14 patients (9.2 percent) presented with Dengue Shock Syndrome (DSS). Notably, we observed that the most prevalent age group among DF cases (52.9 percent) fell within the age range of 21 to 40 years. In contrast, the age group of 41 to 60 years predominated among DHF cases (54.1 percent), and the age group of 61 to 80 years was most frequently associated with DSS cases (57.1 percent). Our analysis revealed a substantial and statistically significant correlation between advancing age and heightened severity of dengue infection (p-value of 0.01, denoting a highly significant statistical association). In a similar investigation conducted by Bandopadhyaya et al. [9], their study encompassed 110 cases, comprising 61 male patients (55.5 percent) and 49 female patients (44.5 percent). Likewise, Rajoo Singh et al. [10] conducted a comparable trial, enrolling a total of 214 participants for their study. Fever emerged as the predominant initial symptom in our study, affecting 76 patients (49.6 percent) upon admission. Other commonly reported presenting symptoms included abdominal discomfort in 70 patients (45.7 percent), rash in 62 patients (40.5 percent), vomiting in 62 patients (39.2 percent), headache in 54 patients (35.2 percent), and joint pain in 51 patients (33.3 percent). According to Bandopadhyaya et al. [9], fever was the predominant presenting symptom in all 110 cases (100 percent), with other frequently observed symptoms including abdominal pain in 52 patients (47.2 percent), vomiting in 44 patients (40 percent), headache in 34 patients (30.9 percent), and joint pain in 63

patients (57.2 percent). In a different study by Kittittrakul et al. [11], all 127 patients (100 percent) presented with fever prior to admission, alongside other symptoms such as abdominal pain in 35 patients (27.5 percent), rash in 20 patients (15.7 percent), vomiting in 107 patients (84.2 percent), headache in 96 patients (75.5 percent), and joint pain in 71 patients (55.9 percent). Notably, Rajoo Singh et al. [10] reported fever as the primary presenting symptom in 214 patients (100 percent) in their study, followed by myalgia in 92 patients (43 percent), vomiting in 80 patients (37.3 percent), and abdominal pain in 43 patients (20 percent).

Our study found that the majority of dengue patients had elevated AST and ALT levels, with a significant increase in severe cases (DHF and DSS). ALP levels remained normal. These findings align with previous research. Elevated AST and ALT levels suggest liver involvement in dengue, possibly due to hepatocyte infection and apoptosis. Histological changes in the liver include fatty alterations, hepatocyte necrosis, and Kupffer cell death, particularly in the midzonal region. The antibody-dependent enhancement hypothesis explains severe dengue risk in secondary infections. Cytokines like interferon, TNF, and IL play crucial roles in severe dengue pathophysiology [12-16].

Conclusion

Heightened levels of AST (Aspartate Transaminase) and ALT (Alanine Transaminase) were notably associated with the severity of Dengue Shock Syndrome (DSS) and Dengue Hemorrhagic Fever (DHF). Furthermore, our investigation revealed that AST levels demonstrated a more significant increase compared to ALT levels among dengue patients. As a result of these findings, we propose a crucial recommendation: individuals diagnosed with dengue infection should undergo an initial liver function test (LFT) and have their liver function

continuously monitored to promptly identify any early signs of hepatic damage.

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