Original Article

Influence of Dengue Fever on Liver Function as Indicated by Aminotransferase Levels

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Abstract

Background: *Dengue fever is a globally prevalent arboviral infection with varied clinical manifestations. Liver involvement is increasingly recognized as a common complication, but its relationship with disease severity remains incompletely understood. This study aimed to evaluate the influence of dengue virus infection on liver function as indicated by aminotransferase levels and to assess their potential as predictors of disease severity.* ***Materials and Methods:*** *This cross-sectional observational study included 100 serologically confirmed dengue patients admitted to Enam medical college hospital. Patients were classified as having dengue fever (DF) or dengue hemorrhagic fever (DHF) according to WHO criteria. Comprehensive clinical assessment and serial laboratory investigations, including liver function tests, were performed. The severity of liver involvement was classified based on aminotransferase levels: Grade A (normal), Grade B (>1-3× upper limit of normal [ULN]), Grade C (>3-10× ULN), and Grade D (>10× ULN).* ***Results:*** *Out of 100 patients, 54% were male and the average age was 36.7 ± 15.2 years. Among them, 72 had dengue fever (DF) and 28 had dengue hemorrhagic fever (DHF). Liver involvement, indicated by elevated aminotransferase levels, was observed in 85% of patients. The median AST and ALT levels were significantly higher in DHF compared to DF patients (AST: 286 vs. 98 IU/L, p<0.001; ALT: 198 vs. 68 IU/L, p<0.001). AST levels exceeded ALT in 87% of cases, with a mean AST/ALT ratio of 1.7±0.6. Severe liver involvement (Grade D) was significantly more common in DHF than DF patients (28.6% vs. 5.6%, p<0.001). The frequency of complications increased significantly with the severity of liver involvement, from 0% in Grade A to 58.3% in Grade D (p<0.001). All patients with elevated aminotransferases showed normalization within 4 weeks without specific hepatoprotective therapy.* ***Conclusion:*** *Liver involvement is a common feature of dengue infection, with a distinctive pattern of AST predominance. The severity of liver involvement correlates significantly with disease severity and clinical outcomes. Despite significant elevations, hepatic involvement in dengue is generally self-limiting. Routine assessment of aminotransferase levels should be considered in the management of dengue patients to identify those at risk of developing severe diseases.*

Keywords: Dengue fever, Liver function, Alanine aminotransferase, Aspartate aminotransferase.
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Introduction

Dengue fever is a prevalent arboviral infection found predominantly in tropical and subtropical regions worldwide, with an estimated 390 million infections annually[1]. The disease is caused by the dengue virus (DENV), which belongs to the Flaviviridae family, with four distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4)[2]. While the majority of infections present as self-limiting febrile illness characterized by high fever, headache, retroorbital pain, myalgia, arthralgia, and rash, a significant proportion can progress to more severe forms, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS)[3]. Although the liver is not the primary target organ for DENV, hepatic involvement is increasingly recognized as a common complication of dengue infection[4]. The inflammatory process resulting from DENV infection can lead to parenchymal lesions that release liver enzymes into the bloodstream[5]. One of the key biochemical indicators of liver involvement in dengue is the elevation of serum aminotransferases- alanine aminotransferase (ALT) and aspartate aminotransferase (AST), with abnormal levels observed in approximately 65 to 97

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percent of cases[6,7]. The degree of liver injury can range from mild elevation of enzymes to acute hepatitis and, rarely, to fulminant hepatic failure[8].

Recent studies suggest that the pattern and severity of aminotransferase elevation may have prognostic significance in dengue infection[9]. Notably, AST levels tend to be higher than ALT in dengue-associated liver injury, which differs from the pattern observed in viral hepatitis[10]. Moreover, there appears to be a correlation between the degree of aminotransferase elevation and disease severity, with significantly higher levels observed in patients with DHF and DSS compared to those with uncomplicated dengue fever[11]. Despite the frequency of liver involvement in dengue infection, the exact pathophysiological mechanisms remain incompletely understood. Direct viral cytopathic effects, immune-mediated injury, hypoxic damage from circulatory compromise, and metabolic acidosis have all been proposed as potential mechanisms[12]. Additionally, pre-existing liver conditions, host genetic factors, and virus serotype may influence the pattern and severity of liver involvement[13].

This study aims to evaluate the impact of dengue fever on liver function by analyzing aminotransferase levels in 100 serologically confirmed dengue cases. We assessed the pattern of enzyme elevation, classified liver involvement severity, and explored correlations with clinical symptoms.

Materials and Methods

Study Design and Population: This cross-sectional observational study was conducted at Enam medical college hospital, Dhaka from August 2024 to January 2025. The study was approved by the Institutional Ethics Committee (Ref: EMC/ERC/2024/08-1), and written informed consent was obtained from all participants or their legal guardians before enrollment. A total of 100 patients with serologically confirmed dengue fever were included in the study.

Inclusion and Exclusion Criteria: Patients with ≥7 years of age and presented with acute febrile illness with two or more of the following symptoms: fever, headache, retroorbital pain, myalgia, arthralgia, skin rash, nausea, vomiting, or hemorrhagic manifestations[14], and had a positive dengue NS1 antigen test and/or positive dengue IgM antibody test. Patients were excluded if they had a history of pre-existing liver disease, alcohol consumption >20 g/day, current or recent (within six months) use of hepatotoxic drugs, positive serological markers for viral hepatitis (HAV, HBV, HCV, or HEV) or had any other confirmed acute infection affecting liver function.

Clinical Assessment: All patients underwent a comprehensive clinical evaluation upon admission and daily during hospitalization. Demographic data, detailed clinical history, and physical examination findings were recorded using a standardized case report form. Patients were classified as having dengue fever (DF) or dengue hemorrhagic fever (DHF) according to the World Health Organization (WHO) 2009 criteria[15]. DHF was diagnosed based on the presence of the following criteria: fever, hemorrhagic manifestations, thrombocytopenia (platelet count <100,000/mm³), and evidence of plasma leakage (hematocrit increase ≥20% from baseline, pleural effusion, or ascites).

Laboratory Investigations: Blood samples were collected from all patients at admission and subsequently at 24-hour intervals until discharge or normalization of laboratory parameters. Complete blood counts, including hemoglobin, hematocrit, total leukocyte count, and platelet count, were performed using an automated hematology analyzer (Sysmex XN-1000). Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were measured using a coagulation analyzer (Sysmex CA-1500). Liver function tests, including serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, direct bilirubin, alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total protein, and albumin, were performed using an automated biochemical analyzer (Beckman Coulter AU5800). The reference ranges for aminotransferases were established according to our laboratory standards: ALT 0-40 IU/L and AST 0-40 IU/L for both males and females.

Serological confirmation of dengue infection was performed using dengue NS1 antigen detection (Dengue NS1 Ag Rapid Test, SD BIOSENSOR) during the first 5 days of illness and/or dengue-specific IgM antibody detection by ELISA (Dengue IgM Capture ELISA) after the 5th day of illness. To exclude other hepatotropic viral infections, serological tests for hepatitis A (anti-HAV IgM), hepatitis B (HBsAg and anti-HBc IgM), hepatitis C (anti-HCV), and hepatitis E (anti-HEV IgM) were performed using commercially available ELISA kits (DiaSorin S.p.A) in all patients with elevated aminotransferase levels.

Assessment of Liver Involvement: The severity of liver involvement was classified based on the peak serum aminotransferase (ALT or AST) levels recorded during illness, according to the criteria modified from Souza et al[5].

- Grade-A: Normal aminotransferase levels
- Grade-B: Mild elevation (>1 to 3 times the upper limit of normal [ULN])

- Grade-C: Moderate elevation (>3 to 10 times ULN)
- Grade-D: Severe elevation (>10 times ULN)

Acute hepatitis was defined as a serum aminotransferase level >10 times the ULN. Acute liver failure was defined as the development of hepatic encephalopathy and coagulopathy (INR ≥1.5) in patients with no pre-existing liver disease and an illness of <26 weeks duration[16].

Abdominal Ultrasonography: Abdominal ultrasonography was performed in all patients with clinical evidence of hepatic involvement (right upper quadrant tenderness, hepatomegaly, or jaundice) or elevated aminotransferase levels using a high-resolution ultrasound machine (Philips EPIQ 7G) by experienced radiologists who were blinded to the clinical and laboratory data[17]. The following parameters were assessed: liver size, echotexture, gallbladder wall thickness, presence of ascites, pleural effusion, and splenomegaly.

Statistical Analysis: Statistical analysis was performed using SPSS version 26.0. Continuous variables were expressed as mean±standard deviation (SD) or median with interquartile range (IQR) depending on the distribution of data. Categorical variables were expressed as frequencies and percentages. The Kolmogorov-Smirnov test was used to assess the normality of data distribution. Comparisons between groups (DF vs. DHF, and different grades of liver involvement) were made using the Student's t-test or Mann-Whitney U test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. The correlation between aminotransferase levels and clinical parameters was evaluated using Pearson's correlation coefficient. A p-value <0.05 was considered statistically significant.

Results

Demographic and Clinical Characteristics: A total of 100 patients with serologically confirmed dengue infection were included in the study. The mean age was 36.7±15.2 years (range: 8-72 years), with a slight male predominance (54; 54%). Based on the WHO criteria, 72 patients (72%) were classified as having dengue fever (DF) and 28 patients (28%) as having dengue hemorrhagic fever (DHF). The most common clinical manifestations were fever (100%), headache (88%), myalgia (86%), and arthralgia (78%). Patients with DHF had a significantly longer duration of fever (6.3±2.0 vs. 4.9±1.6 days, p=0.001) and higher frequency of abdominal pain (78.6% vs. 43.1%, p=0.001), hepatomegaly (64.3% vs. 26.4%, p<0.001), right hypochondrial tenderness (71.4% vs. 34.7%, p<0.001), and jaundice (21.4% vs. 2.8%, p=0.003) compared to patients with DF. All DHF patients (100%) had hemorrhagic manifestations, with petechiae being the most common (78.6%), while only 19.4% of DF patients exhibited any bleeding manifestations (p<0.001). The mean duration of hospital stay was significantly longer in patients with DHF compared to those with DF (7.3±2.6 vs. 4.9±1.8 days, p<0.001) (Table-I).

Laboratory Findings: The hematological and biochemical parameters of the study population are summarized in Table-II. Patients with DHF had significantly lower platelet counts (42.6±18.4 vs. 86.5±32.7×10³/µL, p<0.001) and higher hematocrit values (44.3±4.8 vs. 40.2±3.9%, p<0.001) compared to those with DF. Prothrombin time and activated partial thromboplastin time were significantly prolonged in DHF patients (p<0.001) (Table-II).

Liver Involvement in Dengue Infection: Liver involvement, as indicated by elevated aminotransferase levels, was observed in 85 out of 100 patients (85%). The median AST and ALT levels in the total cohort were 124 IU/L (IQR: 62-248) and 86 IU/L (IQR: 42-182), respectively. Both AST and ALT levels were significantly higher in patients with DHF compared to those with DF (AST: 286 vs. 98 IU/L, p<0.001; ALT: 198 vs. 68 IU/L, p<0.001). Notably, the AST/ALT ratio was >1 in 87% of patients, with a mean ratio of 1.7 ± 0.6, which was significantly higher in DHF patients compared to DF patients (1.9 ± 0.7 vs. 1.6 ± 0.5, p=0.018) (Table-II).

The severity of liver involvement based on aminotransferase levels is presented in Table-III. Among the 85 patients with elevated aminotransferases, 36 (42.4%) had mild elevation (Grade-B), 37 (43.5%) had moderate elevation (Grade-C), and 12 (14.1%) had severe elevation (Grade-D). The frequency of severe liver involvement (Grade-D) was significantly higher in DHF patients compared to DF patients (32.1% vs. 5.6%, p<0.001).

Table-I: Demographic and clinical characteristics of patients with dengue infection (n=100)

Characteristics	Total (n=100)	DF (n=72)	DHF (n=28)	p-value
Demographics				
Age (years), mean ± SD	36.7 ± 15.2	35.4 ± 14.8	39.8 ± 15.9	0.187
Male gender, n (%)	54 (54)	39 (54.2)	15 (53.6)	0.957

Characteristics	Total (n=100)	DF (n=72)	DHF (n=28)	p-value
Clinical features, n (%)				
Fever	100 (100)	72 (100)	28 (100)	1.000
Duration of fever (days), mean ± SD	5.3 ± 1.8	4.9 ± 1.6	6.3 ± 2.0	0.001
Headache	88 (88)	62 (86.1)	26 (92.9)	0.347
Retro-orbital pain	71 (71)	49 (68.1)	22 (78.6)	0.295
Myalgia	86 (86)	60 (83.3)	26 (92.9)	0.213
Arthralgia	78 (78)	54 (75.0)	24 (85.7)	0.239
Rash	51 (51)	34 (47.2)	17 (60.7)	0.217
Nausea/Vomiting	64 (64)	43 (59.7)	21 (75.0)	0.149
Abdominal pain	53 (53)	31 (43.1)	22 (78.6)	0.001
Hepatomegaly	37 (37)	19 (26.4)	18 (64.3)	<0.001
Right hypochondrial tenderness	45 (45)	25 (34.7)	20 (71.4)	<0.001
Jaundice	8 (8)	2 (2.8)	6 (21.4)	0.003
Hemorrhagic manifestations, n (%)				
Any bleeding	42 (42)	14 (19.4)	28 (100)	<0.001
Petechiae	33 (33)	11 (15.3)	22 (78.6)	<0.001
Gum bleeding	12 (12)	2 (2.8)	10 (35.7)	<0.001
Epistaxis	9 (9)	1 (1.4)	8 (28.6)	<0.001
Melena	6 (6)	0 (0)	6 (21.4)	<0.001
Hematemesis	4 (4)	0 (0)	4 (14.3)	0.001
Signs of plasma leakage, n (%)				
Ascites	12 (12)	0 (0)	12 (42.9)	<0.001
Pleural effusion	14 (14)	0 (0)	14 (50.0)	<0.001
Hospital stays (days), mean ± SD	5.6 ± 2.3	4.9 ± 1.8	7.3 ± 2.6	<0.001

Table-II: Laboratory parameters of patients with dengue infection (n=100)

Parameters	Total (n=100)	DF (n=72)	DHF (n=28)	p-value
Hematological parameters				
Hemoglobin (g/dL), mean ± SD	13.2 ± 1.8	13.0 ± 1.7	13.7 ± 1.9	0.076
Hematocrit (%), mean ± SD	41.4 ± 4.5	40.2 ± 3.9	44.3 ± 4.8	<0.001
White blood cell count (×10³/μL), mean ± SD	4.2 ± 2.1	4.5 ± 2.2	3.4 ± 1.6	0.021
Platelet count (× 10³/μL), mean ± SD	74.5 ± 36.3	86.5 ± 32.7	42.6 ± 18.4	<0.001
Prothrombin time (seconds), mean ± SD	14.3 ± 2.8	13.4 ± 2.1	16.7 ± 3.2	<0.001
aPTT (seconds), mean ± SD	38.6 ± 9.3	35.9 ± 7.6	45.8 ± 9.7	<0.001
Liver function tests				
Total bilirubin (mg/dL), mean ± SD	0.9 ± 0.7	0.7 ± 0.4	1.6 ± 1.0	<0.001
Direct bilirubin (mg/dL), mean ± SD	0.4 ± 0.5	0.3 ± 0.2	0.9 ± 0.8	<0.001
AST (IU/L), median (IQR)	124 (62-248)	98 (54-176)	286 (158-468)	<0.001
ALT (IU/L), median (IQR)	86 (42-182)	68 (36-124)	198 (112-342)	<0.001
AST/ALT ratio, mean ± SD	1.7 ± 0.6	1.6 ± 0.5	1.9 ± 0.7	0.018
Alkaline phosphatase (IU/L), mean ± SD	118 ± 52	112 ± 46	134 ± 62	0.054
GGT (IU/L), mean ± SD	76 ± 64	62 ± 48	112 ± 84	<0.001
Total protein (g/dL), mean ± SD	6.7 ± 0.7	6.8 ± 0.6	6.3 ± 0.8	0.001
Albumin (g/dL), mean ± SD	3.8 ± 0.5	4.0 ± 0.4	3.4 ± 0.5	<0.001

Table-III: Severity of Liver involvement based on aminotransferase levels in dengue patients (n=100)

Grade of liver involvement	Total (n=100)	DF (n=72)	DHF (n=28)	p-value
Grade-A (Normal), n (%)	15 (15.0)	14 (19.4)	1 (3.6)	<0.001
Grade-B (>1-3× ULN), n (%)	36 (36.0)	30 (41.7)	6 (21.4)	>0.05
Grade-C (>3-10× ULN), n (%)	37 (37.0)	24 (33.3)	13 (46.4)	>0.05
Grade-D (>10× ULN), n (%)	12 (12.0)	4 (5.6)	8 (28.6)	<0.001

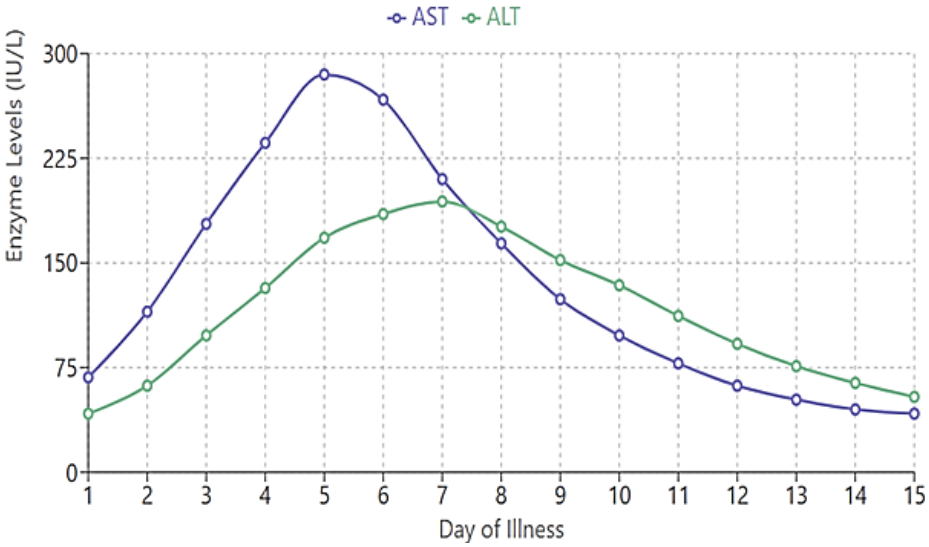

Figure-1: Line graph showing the temporal pattern of mean AST and ALT levels in relation to the day of illness

Table-IV: Correlation Between Aminotransferase Levels and Parameters of Disease Severity

Parameters	AST		ALT	
	r	p-value	r	p-value
Duration of fever	0.582	<0.001	0.524	<0.001
Duration of hospital stay	0.614	<0.001	0.538	<0.001
Platelet count	-0.492	<0.001	-0.465	<0.001
Hematocrit	0.348	<0.001	0.312	0.002
Prothrombin time	0.397	<0.001	0.376	<0.001
Total bilirubin	0.486	<0.001	0.512	<0.001
Albumin	-0.423	<0.001	-0.401	<0.001
Warning signs score*	0.573	<0.001	0.542	<0.001

*Warning signs score: Sum of warning signs present (range: 0-7)

Table-V: Correlation Between Ultrasonographic Findings and Severity of Liver Involvement (n=78)

Ultrasonographic finding	Grade-B (n=32)	Grade-C (n=34)	Grade-D (n=12)	p-value
Hepatomegaly, n (%)	11 (34.4)	18 (52.9)	8 (66.7)	0.037
Hepatic echotexture changes, n (%)	6 (18.8)	14 (41.2)	7 (58.3)	0.012
Gallbladder wall thickening, n (%)	7 (21.9)	14 (41.2)	7 (58.3)	0.024
Ascites, n (%)	1 (3.1)	6 (17.6)	5 (41.7)	0.003
Pleural effusion, n (%)	2 (6.3)	7 (20.6)	5 (41.7)	0.008
Splenomegaly, n (%)	3 (9.4)	6 (17.6)	3 (25.0)	0.210

Table-VI: Relationship between severity of liver involvement and clinical outcomes

Outcome	Grade-A (n=15)	Grade-B (n=36)	Grade-C (n=37)	Grade-D (n=12)	p-value
Complications, n (%)					
Any complication	0 (0)	2 (5.6)	9 (24.3)	7 (58.3)	<0.001
Prolonged thrombocytopenia	0 (0)	1 (2.8)	5 (13.5)	4 (33.3)	0.002
Acute kidney injury	0 (0)	0 (0)	3 (8.1)	3 (25.0)	0.003
Encephalopathy	0 (0)	0 (0)	2 (5.4)	2 (16.7)	0.018
Severe bleeding	0 (0)	0 (0)	2 (5.4)	1 (8.3)	0.134
Duration of hospital stays (days)					
Mean ± SD	3.9 ± 1.2	4.8 ± 1.6	6.3 ± 2.1	8.4 ± 2.9	<0.001

Relationship Between Aminotransferase Levels and Disease Severity: Correlation analysis revealed significant positive correlations between aminotransferase levels and several clinical parameters associated with disease severity (Table-IV). Both AST and ALT levels showed strong positive correlations with the duration of fever, duration of hospital stay, and the presence of warning signs. Additionally, there were moderate negative correlations between aminotransferase levels and platelet count and albumin levels.

Ultrasonographic Findings: Abdominal ultrasonography was performed in 78 patients who had clinical evidence of hepatic involvement or elevated aminotransferase levels. The most common abnormal findings were hepatomegaly (47.4%), gallbladder wall thickening (35.9%), and ascites (15.4%). Table-V shows the correlation between ultrasonographic findings and the severity of liver involvement. The frequency of abnormal ultrasonographic findings increased significantly with increasing aminotransferase levels, particularly in patients with Grade-C and Grade-D liver involvement.

Clinical Outcomes: There were no reported deaths in the study population. However, complications were observed in 18 patients (18%), with significantly higher frequency in those with DHF compared to DF (53.6% vs. 4.2%, $p<0.001$). The most common complications were prolonged thrombocytopenia (10%), acute kidney injury (6%), and encephalopathy (4%). Notably, the frequency of complications increased significantly with the severity of liver involvement (Table-VI). All patients with Grade-D liver involvement showed normalization of aminotransferase levels within 4 weeks of follow-up, with no evidence of chronic liver disease.

Discussion

Demographic and Clinical Characteristics*:* In 100 serologically confirmed dengue cases, this study found liver involvement to be common, with 85% showing elevated aminotransferase levels. Furthermore, the severity of liver involvement, as reflected by higher aminotransferase levels, was significantly associated with dengue hemorrhagic fever (DHF). The demographic and clinical profile of our patients was consistent with previous studies[18]. The mean age of our study (36.7 years) reflects the changing epidemiology of dengue in endemic regions, with an increasing incidence in adults compared to the traditionally affected pediatric population[19]. The slight male predominance (54%) in our study aligns with findings from other endemic areas, possibly due to higher outdoor exposure and healthcare-seeking behavior among males[20].

Fever, headache, myalgia, and arthralgia were the most common clinical manifestations in our patients, consistent with the classical description of dengue fever. However, patients with DHF had a significantly higher frequency of hepatic manifestations, including abdominal pain, hepatomegaly, right hypochondrial tenderness, and jaundice, compared to those with dengue fever (DF). Similar results reported by Samanta et al.[12] and Itha et al.[21] and suggest hepatic involvement may be a key clinical marker of severe dengue.

Patterns of Aminotransferase Elevation in Dengue: Our study revealed that 85% of dengue patients had elevated aminotransferase levels, with AST elevation (83%) being more common than ALT elevation (74%). This pattern aligns with the results of earlier studies. Souza et al.[5] reported abnormal aminotransferase levels in 65.1% of 169 serologically confirmed dengue cases, while Wang et al.[7] in their meta-analysis found that 78% of dengue patients had elevated AST and 71% had elevated ALT levels. The higher frequency of aminotransferase elevation in our study could be attributed to the timing of sample collection and the severity profile of our cohort, with 28% of patients having DHF.

A distinctive pattern observed in our study was that AST levels were consistently higher than ALT levels, with an AST/ALT ratio >1 in 87% of patients. This finding contrasts with the pattern typically observed in viral hepatitis, where ALT elevations usually exceed AST elevations[22]. The disproportionate elevation of AST in dengue could be explained by several mechanisms. First, dengue viruses may cause direct cytopathic effects on hepatocytes, leading to their damage and release of intracellular enzymes[23]. Second, AST is present in various tissues, including cardiac muscle, skeletal muscle, kidneys, brain, and red blood cells, all of which can be affected in dengue infection, potentially contributing to higher AST levels[24]. Third, the release of cytokines and chemokines during the immune response to dengue virus may cause hepatocyte injury and apoptosis, further elevating AST levels[25].

Another interesting observation was the temporal pattern of aminotransferase elevation. AST levels peaked earlier (day 5-6 of illness) compared to ALT levels (day 6-7 of illness), and both gradually decreased thereafter. This trend aligns with the observations reported by Kuo et al.[10], who reported that aminotransferase levels typically peak during the toxic phase of the illness and coincide with the nadir of thrombocytopenia. The earlier peak of AST compared to ALT could reflect the initial involvement of extrahepatic sources of AST,

followed by more specific hepatocellular damage as the infection progresses.

Severity of Liver Involvement in Dengue: This study classified the severity of liver involvement into four grades based on aminotransferase levels. Most patients had mild (36%) to moderate (37%) liver involvement, while severe liver involvement (Grade-D) was observed in 12% of cases. The frequency of severe liver involvement was significantly higher in patients with DHF compared to those with DF (28.6% vs. 5.6%), suggesting a correlation between liver damage and disease severity. Similar findings have been reported by Lee et al.[9], who found that median AST and ALT levels showed a significant increase with the progression of dengue severity. In their study of 690 dengue patients in Singapore, 7 patients (1%) had AST or ALT ≥1000 IU/L, comparable to our finding of 12% with Grade-D liver involvement. The higher proportion in our study might be related to differences in the study population, viral serotypes, or genetic factors that influence the host response to infection.

It is noteworthy that despite significant amino-transferase elevations, none of our patients developed acute liver failure, and all showed normalization of liver enzymes within 4 weeks of follow-up. This observation is consistent with the generally self-limiting nature of hepatic involvement in dengue infection reported by Fernando et al[13]. However, it is important to acknowledge that severe and even fatal hepatic complications have been documented in dengue, particularly in endemic regions with circulating DENV-3 and DENV-4 serotypes[26].

Correlation with Disease Severity and Clinical Outcomes: Our study demonstrated significant positive correlations between aminotransferase levels and several parameters of disease severity, including the duration of fever, duration of hospital stays, and the presence of warning signs. Additionally, aminotransferase levels showed moderate negative correlations with platelet count and albumin levels. These findings aligned with those of Kalluru et al[11], who reported that elevated liver enzymes were associated with prolonged hospitalization and a more complicated clinical course in dengue patients.

Our study further supported the link between aminotransferase levels and clinical outcomes, showing a significant rise in complications with increasing liver involvement. None of the patients with normal aminotransferase levels (Grade-A) developed complications, whereas 58.3% of those with severe liver involvement (Grade-D) experienced at least one complication, most commonly prolonged thrombocytopenia, acute kidney injury, and encephalopathy. This observation underscores the systemic nature of severe dengue infection and the role of liver dysfunction as both a marker and a contributor to disease complications.

Pathophysiological Mechanisms of Liver Involvement in Dengue: The precise mechanisms of liver injury in dengue infection remain incompletely understood, but several pathways have been proposed. Direct viral invasion of hepatocytes has been demonstrated by the detection of dengue virus antigens in liver tissue samples[27]. Autopsy studies have shown evidence of hepatocellular necrosis, Councilman bodies, and micro vesicular steatosis in fatal dengue cases[28]. Additionally, immunological mechanisms, including the release of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-10, may contribute to liver damage through induction of oxidative stress and apoptosis[23].

The ultrasonographic findings in our study correlated well with the severity of liver involvement based on aminotransferase levels. Hepatomegaly, hepatic echotexture changes, and gallbladder wall thickening were significantly more common in patients with higher aminotransferase levels. These findings agree with those of Motla et al[17], who reported that sonographic evidence of hepatomegaly and gallbladder wall thickening had high positive predictive values for severe dengue. Ultrasonography thus provides a valuable non-invasive tool for assessing the extent of visceral involvement in dengue infection, especially in environments with limited laboratory resources.

Clinical Implications: Our study's findings carry several significant clinical implications. First, they highlight the need for routine assessment of aminotransferase levels in all dengue patients, regardless of the presence of overt hepatic symptoms. Early identification of patients with significant liver involvement could facilitate prompt interventions and closer monitoring.

Second, the observation that all patients with elevated aminotransferases, including those with severe elevations, showed normalization of liver enzymes within 4 weeks without specific hepatoprotective therapy underscores the generally benign and self-limiting nature of hepatic involvement in dengue. This information can be reassuring for both healthcare providers and patients. Finally, our findings regarding the relationship between aminotransferase levels and clinical outcomes suggest that the severity of liver involvement could influence management decisions, such as the need for hospitalization, frequency of monitoring, and nutritional support. Patients with significant liver involvement may

benefit from a more conservative approach to fluid management and cautious use of potentially hepatotoxic medications.

Limitations

First, the sample size was only 100 which limits the generalizability of our findings. Second, the absence of liver biopsies precludes definitive correlation between aminotransferase elevations and histopathological changes. Third, our study did not assess the potential contribution of concurrent medications, including antipyretics and antibiotics, to aminotransferase elevations. Fourth, the follow-up period of 4 weeks may not be sufficient to detect potential long-term hepatic sequelae.

Conclusion

Our study showed that liver involvement was common in dengue infection, with elevated aminotransferase levels observed in 85% of cases. The median AST and ALT levels were significantly higher in DHF compared to DF patients. Despite significant aminotransferase elevations, liver involvement is usually self-limiting, with normalization within four weeks. These findings underscore the importance of routine assessment of aminotransferase levels in the management of dengue patients and provide additional insights into the pathophysiology of this global health challenge.

Recommendations

Longitudinal studies with longer follow-up could better define how liver enzymes normalize over time and identify factors linked to persistent liver dysfunction. Mechanistic research using liver biopsies, viral load data, and cytokine profiles may deepen understanding of dengue-related liver injury. Research should also explore how comorbidities like chronic liver disease and obesity affect liver involvement. Additionally, investigating the correlation between aminotransferase levels and emerging biomarkers such as NS1 antigen, soluble CD163, and microRNAs may offer new insights into disease severity and progression.

Conflict of interest

The authors declared that they have no conflict of interests.

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