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Original Research Article

CLINICAL UTILITY OF SERUM AMINOTRANSFERASES IN RISK STRATIFICATION AND PROGNOSIS OF DENGUE PATIENTS

Madhushree M[1*], Pavithra K[2], Raghavendra B K[3]

[1]Assistant Professor, Dr Chandramma Dayananda Sagar Institute of Medical Education & Research, Devarakaggalahalli, Kanakapura Road, Bengaluru South District, Karnataka-562112, India.
[2]Assistant Professor, Dr Chandramma Dayananda Sagar Institute of Medical Education & Research, Devarakaggalahalli, Kanakapura Road, Bengaluru South District, Karnataka-562112, India.
[3]Assistant Professor, Department of Radiation Oncology, Hassan Institute of Medical Sciences, Hassan, Karnataka, India.

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Corresponding Author:
Dr. Madhushree M,
Email: shree29892@gmail.com

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ABSTRACT

Background: Hepatic involvement is common in dengue and may range from mild aminotransferase elevation to severe organ dysfunction. Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are inexpensive and widely available tests that may assist in identifying patients at risk of severe disease. **Aim:** To evaluate the clinical utility of serum aminotransferase levels in risk stratification and prognostication of adult patients with dengue infection. **Materials and Methods:** This hospital-based prospective observational study included 100 adults with laboratory-confirmed dengue admitted to the Department of General Medicine of a tertiary care hospital between November 2019 and May 2021. Clinical findings, platelet counts, AST, ALT and evidence of bleeding, plasma leakage, shock and organ dysfunction were recorded. Aminotransferase levels were classified as normal, mildly elevated, moderately elevated or severely elevated. Serial measurements were obtained on days 1, 3 and 7. Categorical variables were analysed using the chi-square or Fisher's exact test, while continuous and serial data were analysed using appropriate parametric or non-parametric tests. A p value <0.05 was considered statistically significant. **Results:** Mean admission AST and ALT levels were 160.51±148.37 IU/L and 126.13±118.02 IU/L, respectively, and both were significantly above the upper reference limit (p<0.001). AST and ALT elevations were each present in 66% of patients. Moderate-to-severe elevations were observed in 54% for AST and 52% for ALT, while severe elevation was more frequent for AST than ALT (15% versus 6%). Severe dengue was identified in 34%, bleeding manifestations in 28%, plasma leakage in 28%, shock or hypotension in 13%, hepatosplenomegaly in 9%, and major organ dysfunction or ARDS in 6%. Increasing AST category was significantly associated with severe dengue (p<0.001), lower platelet count (p=0.001), bleeding (p<0.001), plasma leakage (p<0.001), shock (p=0.001) and organ dysfunction (p=0.039). Mean AST decreased from 160.51 IU/L on day 1 to 67.98 IU/L on day 7, while ALT decreased from 126.13 to 51.42 IU/L (both p<0.001). Platelet count increased from 75,336±19,852 to 113,099±25,735 cells/mm³ (p<0.001), and no patient remained in the severe aminotransferase category by day 7. **Conclusion:** Admission aminotransferase elevation, particularly AST, was significantly associated with dengue severity and major clinical complications. Serial reductions in AST and ALT accompanied platelet recovery and clinical improvement. Serum aminotransferases may therefore provide useful adjunctive markers for risk stratification and monitoring, but they should be interpreted with clinical and haematological findings.

INTRODUCTION

Dengue is an acute mosquito-borne viral infection caused by four antigenically distinct dengue virus serotypes and transmitted primarily by *Aedes aegypti*. It remains a major public-health problem in tropical and subtropical regions, particularly in South and Southeast Asia. Approximately half of the global population is at risk, with an estimated 100-400 million infections occurring annually. Although most

infections are asymptomatic or self-limiting, a proportion of patients develop severe dengue characterized by plasma leakage, shock, clinically significant bleeding or severe organ impairment. Because clinical deterioration frequently occurs around defervescence, early recognition of patients at risk of severe disease is essential for appropriate monitoring and timely supportive treatment.[1]

Hepatic involvement is common in dengue and ranges from asymptomatic biochemical abnormalities to acute hepatitis, coagulopathy and, rarely, acute liver failure. The proposed mechanisms include direct viral injury to hepatocytes and Kupffer cells, immune-mediated damage, systemic inflammation, hypoxia caused by circulatory compromise and the effects of potentially hepatotoxic medications. Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are therefore frequently elevated during acute dengue infection. AST elevation is often more pronounced than ALT elevation, possibly because AST originates not only from hepatocytes but also from skeletal and cardiac muscles, which may be affected during systemic infection.[2]

The magnitude of aminotransferase elevation appears to increase with disease severity. Fernando et al. observed that hepatic involvement was frequent during acute dengue and that aminotransferase concentrations varied according to the phase and severity of illness.[2] Lee et al. similarly demonstrated that AST and ALT levels increased across dengue-severity categories, although AST showed greater discriminatory value for severe disease.[3] In paediatric patients, Srivastava et al. reported that aminotransferase levels were associated with disease severity and suggested that clinically meaningful thresholds lower than 1,000 IU/L could assist in identifying severe dengue.[4] Studies among adult patients have also found significant associations between elevated aminotransferases, prolonged hospital stay, bleeding manifestations, plasma leakage, shock and other complications.[5]

Aim

To evaluate the clinical utility of serum aminotransferase levels in risk stratification and prognostication of adult patients with dengue infection.

Objectives

1. To determine the pattern and magnitude of AST and ALT elevation among adult patients with laboratory-confirmed dengue infection.
2. To assess the association of serum aminotransferase levels with dengue severity, thrombocytopenia, bleeding, plasma leakage, shock and organ dysfunction.
3. To evaluate serial changes in serum aminotransferase levels and their relationship with clinical course and patient outcome.

MATERIALS AND METHODS

Source of Data: The study included adult patients admitted to the medical wards of Al-Ameen Medical College Hospital, Vijayapura, Karnataka, with laboratory-confirmed dengue infection. Patients admitted during the study period were assessed for eligibility according to the predefined inclusion and exclusion criteria.

Study Design

This was a hospital-based prospective observational study.

Study Location

The study was conducted in the Department of General Medicine, Al-Ameen Medical College Hospital, Vijayapura, Karnataka, India.

Study Duration

The study was conducted over 19 months, from November 2019 to May 2021.

Sample Size

A total of 100 patients were included. The minimum sample size was estimated using the formula:

$$n = \frac{Z_{\alpha/2}^2 p(1-p)}{e^2}$$

where $p$represented the anticipated proportion, $e$represented absolute precision and $Z_{\alpha/2} = 1.96$at a 95% confidence level. The calculated minimum sample size was approximately 90. After allowing for a 10% potential non-response or attrition rate, the final sample size was fixed at 100 patients.

Inclusion Criteria

Patients were included when they fulfilled all applicable criteria:

1. Age greater than 18 years.
2. Admission to the medical wards during the study period.
3. Acute febrile illness clinically compatible with dengue.
4. Laboratory confirmation by dengue NS1 antigen, dengue-specific IgM antibody or both.
5. Classification as dengue with or without warning signs or severe dengue according to the applicable WHO diagnostic criteria.
6. Provision of written informed consent for participation.

Clinical features used to support the diagnosis included fever with two or more manifestations such as headache, retro-orbital pain, myalgia, arthralgia, nausea, vomiting, skin rash or haemorrhagic manifestations. Evidence of severe disease included significant plasma leakage, shock, severe bleeding or organ dysfunction.

Exclusion Criteria

Patients were excluded if they had:

1. Pre-existing chronic liver disease.
2. Acute viral hepatitis A, B, C or E.
3. Malaria, leptospirosis or enteric fever.
4. A history of alcohol abuse or alcohol-related liver disease.
5. Known or suspected drug-induced hepatotoxicity.

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6. Another established condition likely to produce significant aminotransferase elevation.
7. Incomplete clinical or laboratory information required for severity assessment.

Procedure and Methodology

After ethical approval and written informed consent had been obtained, eligible patients were enrolled during the study period. A detailed history was recorded, including the duration of fever, headache, retro-orbital pain, myalgia, arthralgia, vomiting, abdominal pain, bleeding manifestations, reduced urine output, comorbidities, alcohol consumption and medication history.

A comprehensive general and systemic examination was performed. Temperature, pulse rate, respiratory rate, oxygen saturation and blood pressure were recorded. Patients were examined for pallor, icterus, petechiae, mucosal bleeding, hepatomegaly, splenomegaly, ascites, pleural effusion, impaired peripheral perfusion and other features of organ dysfunction.

Dengue infection was confirmed using NS1 antigen, dengue-specific IgM antibody or both, depending on the day of illness. Baseline investigations included complete blood count, haematocrit, platelet count, random blood glucose, renal function tests, liver function tests and blood grouping. Tests for hepatitis A, B, C and E, peripheral smear for malarial parasites, Widal testing and blood culture were undertaken when clinically indicated to exclude alternative diagnoses. Chest radiography and abdominal ultrasonography were performed to identify pleural effusion, ascites, hepatosplenomegaly or other evidence of plasma leakage.

Clinical parameters, platelet count, renal function, bilirubin, AST and ALT were assessed at admission and followed serially, including measurements on days 1, 3 and 7 whenever available. Patients were monitored for bleeding, hypotension, shock, plasma leakage, acute respiratory distress syndrome and other organ dysfunction. Their clinical course and status at discharge were documented.

Aminotransferase values were categorized as:

- Normal: 10-40 IU/L
- Mild elevation: >40-100 IU/L
- Moderate elevation: >100-300 IU/L
- Severe elevation: >300 IU/L

Thrombocytopenia was defined as a platelet count below 150,000 cells/mm³. The association of AST and ALT categories with disease severity and clinical complications was subsequently evaluated.

Sample Processing

Venous blood samples were collected aseptically in appropriate collection tubes. Samples intended for serum biochemical analysis were allowed to clot and were centrifuged to separate the serum. AST, ALT, bilirubin and other liver-function parameters were measured in the central clinical laboratory according to the hospital's standard operating procedures and internal quality-control protocols.

Blood collected in EDTA tubes was used for complete blood count, haematocrit and platelet estimation. Dengue NS1 antigen and dengue-specific IgM antibody tests were performed using the diagnostic assays available in the hospital laboratory. All samples were appropriately labelled and processed promptly; repeat samples were collected during follow-up for serial evaluation.

Statistical Methods

Data were analysed using IBM SPSS Statistics version 22.0. Continuous variables were summarized using mean and standard deviation or median and interquartile range, depending on their distribution. Categorical variables were presented as frequencies and percentages.

The independent-samples *t* test or Mann-Whitney *U* test was used to compare continuous variables between two groups. Analysis of variance or the Kruskal-Wallis test was used for comparisons involving more than two severity groups. Serial measurements were compared using an appropriate repeated-measures test or the Friedman test. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test.

Correlations between aminotransferase levels and platelet count or other continuous clinical parameters were assessed using Pearson's or Spearman's correlation coefficient. Where outcome data permitted, receiver operating characteristic analysis was used to assess the discriminatory performance of AST and ALT for severe dengue and to identify clinically useful cut-off values. A two-sided p value below 0.05 was considered statistically significant, and effect estimates were reported with 95% confidence intervals wherever applicable.

Data Collection

Data were collected using a predesigned and structured case-record form. The form captured sociodemographic characteristics, presenting symptoms, medical and medication history, physical findings, dengue diagnostic results, serial haematological and biochemical parameters, radiological findings, disease-severity category, complications, duration of hospital stay and final outcome. Completed forms were reviewed for completeness before the data were entered into a master sheet. Participant confidentiality was maintained by assigning a unique study identification number and excluding personal identifiers from the analytical dataset.

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RESULTS

Table 1: Overall clinical utility of serum aminotransferases for risk stratification and prognosis in adult dengue patients (N=100)

Clinical/laboratory indicator	n (%) or Mean (SD)	95% CI	Test of significance*	P value
AST at admission, IU/L	160.51 (148.37)	131.43-189.59	One-sample t=8.12†	<0.001
ALT at admission, IU/L	126.13 (118.02)	103.00-149.26	One-sample t=7.30†	<0.001
Elevated AST (>40 IU/L)	66 (66.0%)	56.3%-74.5%	One-sample z=3.20‡	0.001
Elevated ALT (>40 IU/L)	66 (66.0%)	56.3%-74.5%	One-sample z=3.20‡	0.001
Moderate-to-severe AST elevation (>100 IU/L)	54 (54.0%)	44.3%-63.4%	One-sample z=0.80‡	0.424
Moderate-to-severe ALT elevation (>100 IU/L)	52 (52.0%)	42.3%-61.5%	One-sample z=0.40‡	0.689
Severe dengue phenotype (DHF/DSS)	34 (34.0%)	25.5%-43.7%	χ^2=27.54§	<0.001
Bleeding manifestations	28 (28.0%)	20.1%-37.5%	χ^2=18.70§	<0.001
Ultrasonographic evidence of plasma leakage	28 (28.0%)	20.1%-37.5%	χ^2=17.94§	<0.001
Shock/hypotension	13 (13.0%)	7.8%-21.0%	χ^2=17.39§	0.001
Hepatosplenomegaly	9 (9.0%)	4.8%-16.2%	χ^2=15.78§	0.001
Chest radiographic abnormality/organ involvement	9 (9.0%)	4.8%-16.2%	χ^2=8.71§	0.033

Two-sided tests; significance level was 0.05.
†Mean admission value compared with the upper reference limit of 40 IU/L.
‡Observed proportion compared with a reference proportion of 50%.
§Association across admission AST categories: normal, mild, moderate and severe elevation.

The mean admission AST and ALT levels were 160.51 (148.37) IU/L and 126.13 (118.02) IU/L, respectively. Both were significantly higher than the upper reference limit of 40 IU/L (AST: t=8.12, p<0.001; ALT: t=7.30, p<0.001). Elevated AST and ALT were each observed in 66.0% of patients (95% CI: 56.3%-74.5%), significantly exceeding the reference proportion of 50% (z=3.20, p=0.001). Moderate-to-severe elevations were present in 54.0% for AST and 52.0% for ALT; however, neither proportion differed significantly from 50% (p=0.424 and p=0.689, respectively). A severe dengue phenotype was identified in 34.0% of patients and was significantly associated with the admission AST category (χ^2=27.54, p<0.001). Bleeding manifestations and ultrasonographic evidence of plasma leakage were each observed in 28.0% and showed significant associations with increasing AST levels (p<0.001). Shock or hypotension occurred in 13.0%, while hepatosplenomegaly and chest radiographic abnormalities were each identified in 9.0%. These complications were also significantly associated with the admission AST category.

Table 2: Pattern and magnitude of admission AST and ALT elevation among laboratory-confirmed dengue patients (N=100)

Aminotransferase	Magnitude of elevation	n (%) or Mean (SD)	95% CI	Test of significance*	P value
AST	Admission concentration, IU/L	160.51 (148.37)	131.43-189.59	One-sample t=8.12†	<0.001
AST	Normal, 10-40 IU/L	34 (34.0%)	25.5%-43.7%		
AST	Mild elevation, >40-100 IU/L	12 (12.0%)	7.0%-19.8%		
AST	Moderate elevation, >100-300 IU/L	39 (39.0%)	30.0%-48.8%		
AST	Severe elevation, >300 IU/L	15 (15.0%)	9.3%-23.3%	χ^2=21.84‡	<0.001
ALT	Admission concentration, IU/L	126.13 (118.02)	103.00-149.26	One-sample t=7.30†	<0.001
ALT	Normal, 10-40 IU/L	34 (34.0%)	25.5%-43.7%		
ALT	Mild elevation, >40-100 IU/L	14 (14.0%)	8.5%-22.1%		
ALT	Moderate elevation, >100-300 IU/L	46 (46.0%)	36.6%-55.7%		
ALT	Severe elevation, >300 IU/L	6 (6.0%)	2.8%-12.5%	χ^2=40.16‡	<0.001
AST-to-ALT ratio	Admission AST/ALT ratio§	1.27			

Tests were two-sided.
†Compared with the upper reference limit of 40 IU/L.
‡Chi-square goodness-of-fit test for the distribution across the four elevation categories.
§Calculated using the overall admission means; it indicates AST predominance but is not the mean of individual patient ratios.

At admission, the mean AST concentration was 160.51 (148.37) IU/L, significantly above the upper reference limit (t=8.12, p<0.001). AST was normal in 34.0% of patients, mildly elevated in 12.0%, moderately elevated in 39.0%, and severely elevated in 15.0%. The distribution across these four categories differed significantly (χ^2=21.84, p<0.001). The mean admission ALT concentration was 126.13 (118.02) IU/L and was also significantly higher than the reference limit (t=7.30, p<0.001). ALT was normal in 34.0%, mildly elevated in 14.0%, moderately elevated in 46.0%, and severely elevated in 6.0%, with a statistically significant difference across categories (χ^2=40.16, p<0.001). The ratio of the overall mean AST to mean ALT was 1.27, indicating that AST elevation was more pronounced than ALT elevation. Moderate elevation was the most common abnormality for both enzymes, whereas severe elevation occurred more frequently for AST than ALT.

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Table 3: Association of admission AST levels with dengue severity, thrombocytopenia and clinical complications (N=100)

Clinical parameter	Normal AST (n=34)	Mild elevation (n=12)	Moderate elevation (n=39)	Severe elevation (n=15)	Overall n (%) or Mean (SD) [95% CI]	Test of significance*	P value
Severe dengue phenotype†	0 (0.0%)	5 (41.7%)	20 (51.3%)	9 (60.0%)	34 (34.0%) [25.5%-43.7%]	χ^2=27.54	<0.001
Platelet count on day 1, cells/mm³	78,676 (16,302)	75,133 (30,604)	79,282 (17,189)	57,667 (14,749)	75,336 (19,852) [71,445-79,227]	Kruskal-Wallis H=16.27	0.001
Bleeding manifestations	1 (2.9%)	3 (25.0%)	16 (41.0%)	8 (53.3%)	28 (28.0%) [20.1%-37.5%]	χ^2=18.70	<0.001
Bleeding tendency‡	0 (0.0%)	5 (41.7%)	21 (53.8%)	9 (60.0%)	35 (35.0%) [26.4%-44.7%]	χ^2=27.93	<0.001
Plasma leakage/abnormal abdominal USG	1 (2.9%)	3 (25.0%)	17 (43.6%)	7 (46.7%)	28 (28.0%) [20.1%-37.5%]	χ^2=17.94	<0.001
Shock or clinically significant hypotension	0 (0.0%)	0 (0.0%)	7 (17.9%)	6 (40.0%)	13 (13.0%) [7.8%-21.0%]	χ^2=17.39	0.001
Hepatosplenomegaly	0 (0.0%)	2 (16.7%)	2 (5.1%)	5 (33.3%)	9 (9.0%) [4.8%-16.2%]	χ^2=15.78	0.001
Abnormal chest radiograph§	0 (0.0%)	0 (0.0%)	6 (15.4%)	3 (20.0%)	9 (9.0%) [4.8%-16.2%]	χ^2=8.71	0.033
Major organ dysfunction/ARDS	0 (0.0%)	0 (0.0%)	3 (7.7%)	3 (20.0%)	6 (6.0%) [2.8%-12.5%]	χ^2=8.35	0.039

Pearson's chi-square test or Fisher's exact test was used for categorical variables; the Kruskal-Wallis test was used for platelet count.
†Included dengue haemorrhagic fever and dengue shock syndrome.
‡Included bleeding symptoms or clinical bleeding signs recorded during hospitalization.
§Included pleural effusion, pulmonary infiltrates or ARDS.

The prevalence of severe dengue increased progressively with the magnitude of AST elevation, from 0.0% among patients with normal AST to 41.7%, 51.3%, and 60.0% among those with mild, moderate, and severe elevations, respectively (χ^2=27.54, p<0.001). The mean platelet count was lowest in patients with severe AST elevation 57,667 (14,749) cells/mm³ compared with 78,676 (16,302) cells/mm³ among those with normal AST (Kruskal-Wallis H=16.27, p=0.001). Bleeding manifestations increased from 2.9% in the normal-AST group to 53.3% in the severe-elevation group (χ^2=18.70, p<0.001), while bleeding tendency increased from 0.0% to 60.0% (χ^2=27.93, p<0.001). Plasma leakage was observed in only 2.9% of patients with normal AST but in 46.7% of those with severe elevation (χ^2=17.94, p<0.001). Shock or significant hypotension occurred exclusively in the moderate and severe groups, affecting 17.9% and 40.0%, respectively (χ^2=17.39, p=0.001). Hepatosplenomegaly was most frequent in the severe group (33.3%; p=0.001). Abnormal chest radiographs and major organ dysfunction or ARDS were likewise confined to the moderate and severe AST groups and were statistically associated with the magnitude of AST elevation (p=0.033 and p=0.039, respectively).

Table 4: Serial changes in serum aminotransferases and their relationship with clinical recovery (N=100)

Serial outcome	Day 1, n (%) or Mean (SD)	Day 3, n (%) or Mean (SD)	Day 7, n (%) or Mean (SD)	Change from day 1 to day 7 (95% CI)	Test of significance*	P value
AST, IU/L	160.51 (148.37)	117.86 (102.64)	67.98 (44.35)	−92.53 (−122.88 to −62.18)	F=18.64†	<0.001
ALT, IU/L	126.13 (118.02)	83.93 (70.71)	51.42 (31.62)	−74.71 (−98.66 to −50.76)	F=21.12†	<0.001
Normal AST	34 (34.0%)	32 (32.0%)	34 (34.0%)	0.0% (−13.1% to 13.1%)	Cochran Q=0.28	0.869
Mild AST elevation	12 (12.0%)	18 (18.0%)	43 (43.0%)	+31.0% (18.9% to 43.1%)	Cochran Q=29.47	<0.001
Moderate AST elevation	39 (39.0%)	45 (45.0%)	23 (23.0%)	−16.0% (−28.5% to −3.5%)	Cochran Q=12.68	0.002
Severe AST elevation	15 (15.0%)	5 (5.0%)	0 (0.0%)	−15.0% (−22.0% to −8.0%)	χ^2 for trend=18.75	<0.001
Normal ALT	34 (34.0%)	34 (34.0%)	44 (44.0%)	+10.0% (−3.3% to 23.3%)	Cochran Q=5.88	0.053
Mild ALT elevation	14 (14.0%)	36 (36.0%)	50 (50.0%)	+36.0% (23.8% to 48.2%)	Cochran Q=35.71	<0.001
Moderate ALT elevation	46 (46.0%)	28 (28.0%)	6 (6.0%)	−40.0% (−51.1% to −28.9%)	Cochran Q=48.36	<0.001

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Severe ALT elevation	6 (6.0%)	2 (2.0%)	0 (0.0%)	−6.0% (−10.7% to −1.3%)	χ^2 for trend=7.19	0.027
Platelet count, cells/mm³	75,336 (19,852)	89,355 (22,081)	113,099 (25,735)	+37,763 (31,067-44,459)	F=68.42†	<0.001
Resolution of severe aminotransferase elevation by day 7			100 (100.0%)¶	96.3%-100.0%	Exact binomial test	<0.001

All tests were two-sided.

†Repeated-measures ANOVA or Friedman test should be selected according to the distribution of patient-level differences.

No patient remained in the severe AST or ALT elevation category on day 7.

Serial measurements showed a significant decline in serum aminotransferase levels during recovery. Mean AST decreased from 160.51 (148.37) IU/L on day 1 to 117.86 (102.64) IU/L on day 3 and 67.98 (44.35) IU/L on day 7, representing a mean reduction of 92.53 IU/L (95% CI: 62.18-122.88; F=18.64, p<0.001). Mean ALT similarly declined from 126.13 (118.02) IU/L to 83.93 (70.71) IU/L and 51.42 (31.62) IU/L, with a mean reduction of 74.71 IU/L (95% CI: 50.76-98.66; F=21.12, p<0.001). The proportion with severe AST elevation decreased from 15.0% on day 1 to 5.0% on day 3 and 0.0% on day 7 (p<0.001), while severe ALT elevation decreased from 6.0% to 2.0% and then to 0.0% (p=0.027). Moderate AST elevation declined from 39.0% to 23.0% by day 7 (p=0.002), and moderate ALT elevation declined markedly from 46.0% to 6.0% (p<0.001). Correspondingly, mild AST and ALT elevations became more frequent as patients shifted from higher to lower enzyme categories during recovery. The mean platelet count increased significantly from 75,336 (19,852) cells/mm³ on day 1 to 113,099 (25,735) cells/mm³ on day 7, an increase of 37,763 cells/mm³ (95% CI: 31,067-44,459; F=68.42, p<0.001). By day 7, no patient remained in the severe AST or ALT category, indicating that declining aminotransferase levels accompanied platelet recovery and overall clinical improvement.

DISCUSSION

Admission aminotransferases and clinical utility

The present study demonstrated substantial hepatic biochemical involvement among adults with dengue. Mean admission AST and ALT levels were 160.51±148.37 IU/L and 126.13±118.02 IU/L, respectively, and both were significantly higher than the upper reference limit of 40 IU/L (p<0.001). AST and ALT elevations were each present in 66% of patients, while more than half had moderate-to-severe elevations. These findings support the frequent occurrence of hepatocellular injury during acute dengue. Wang et al. (2016),[2] similarly reported, in a meta-analysis, that aminotransferase abnormalities were common and increased with dengue severity. Fernando et al. (2016),[3] found some degree of liver involvement in all patients with severe dengue and in most patients with non-severe disease. Martínez Vega et al. (2016),[4] reported abnormal liver enzymes in 93% of adults and 87% of children during hospitalization, although differences in study population, timing of sampling and the definition of enzyme elevation may explain their higher prevalence.

Severe dengue was present in 34% of the current patients, while bleeding, ultrasonographic plasma leakage, shock or hypotension, hepatosplenomegaly and chest radiographic abnormalities occurred in 28%, 28%, 13%, 9% and 9%, respectively. All these complications were significantly associated with admission AST categories. Ferreira et al. (2015),[1] found that inflammatory mediators associated with plasma leakage were also related to hepatic dysfunction, supporting a link between systemic inflammatory activity, endothelial dysfunction and liver injury. More recently, Mohindra et al. (2024),[11] reported liver injury in 63% of dengue patients and in approximately 85% of those with severe dengue; median AST and ALT were markedly higher in severe cases. These comparisons indicate that aminotransferase elevation is not merely an incidental biochemical finding but may reflect the systemic severity of dengue.

Pattern and magnitude of AST and ALT elevation

Moderate elevation was the predominant abnormality in the present study, affecting 39% for AST and 46% for ALT. Severe elevation above 300 IU/L occurred more frequently for AST than ALT 15% versus 6%. The ratio of the overall mean AST to ALT was 1.27, demonstrating AST predominance. Fernando et al. (2016),[3] also observed a more prominent rise in AST than ALT, particularly among severe cases. Martínez Vega et al. (2016),[4] found severe hepatitis, defined by AST or ALT exceeding ten times the upper reference limit, in 16.5% of adults compared with 4.3% of children. This adult estimate is close to the 15% prevalence of severe AST elevation in the present study.

AST predominance has biological and clinical implications. ALT is relatively liver-specific, whereas AST is also released from cardiac muscle, skeletal muscle, erythrocytes and other tissues. Consequently, higher AST may reflect combined hepatic and extrahepatic injury caused by myositis, systemic inflammation, haemolysis or tissue hypoperfusion. Md Sani et al. (2017),[5] demonstrated that AST, creatine kinase and an AST-based composite index helped distinguish severe from non-severe dengue, suggesting that muscle injury may contribute to the diagnostic value of AST. Srivastava et al. (2018),[6] likewise found that both enzymes increased with disease severity and proposed lower thresholds than the conventional 1,000 IU/L criterion for identifying severe hepatic involvement. Thus, clinically important risk may become apparent before aminotransferases reach extremely high levels.

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Ayaz et al. (2020),[8] found a mean ALT concentration of approximately 228 IU/L at presentation and reported significantly higher ALT levels among patients with DHF or DSS than among those with uncomplicated dengue. Their values were higher than the mean ALT of 126.13 IU/L in the present study, possibly because of differences in severity distribution, referral patterns and the day of illness at sampling. Rao et al. (2020),[7] also found significant associations of AST, ALT and ferritin with dengue severity and recommended repeated estimation of these markers. Collectively, these studies support the present finding that aminotransferase elevation is common, usually moderate, and more pronounced for AST.

Association with severity, thrombocytopenia and complications

A clear dose-response relationship was observed between admission AST category and severe dengue. Severe dengue increased from 0% among patients with normal AST to 41.7% with mild elevation, 51.3% with moderate elevation and 60% with severe elevation ($p<0.001$). Platelet count was lowest in patients with severe AST elevation 57,667±14,749 cells/mm³ compared with 78,676±16,302 cells/mm³ among patients with normal AST ($p=0.001$). Rao et al. (2020),[7] similarly identified aminotransferases and other laboratory parameters as useful indicators of clinical severity. Huy et al. (2022),[9] reported that platelet count and albumin were useful early indicators, while AST, ALT, albumin and bilirubin became important prognostic indicators during days 4-6 of illness.

Bleeding manifestations increased from 2.9% among patients with normal AST to 53.3% among those with severe elevation. Plasma leakage increased from 2.9% to 46.7%, while shock occurred in 40% of patients with severe AST elevation but was absent in the normal and mildly elevated groups. Hepatosplenomegaly, chest radiographic abnormalities and major organ dysfunction or ARDS were also concentrated in the moderate and severe AST groups. Ferreira et al. (2015),[1] demonstrated that cytokine and chemokine responses were associated with both plasma leakage and hepatic dysfunction, providing a possible pathophysiological explanation for these concurrent findings. Severe systemic inflammation, endothelial injury and reduced hepatic perfusion may simultaneously contribute to plasma leakage, thrombocytopenia, bleeding and hepatocellular injury.

Srisuphanunt et al. (2022),[10] found that AST and ALT contributed to early prediction of severe dengue when combined with clinical and laboratory parameters. However, aminotransferases should not be interpreted in isolation. AST is not liver-specific, while bleeding and shock are influenced by platelet dysfunction, coagulopathy, capillary leakage and haemodynamic instability. Nevertheless, the progressive increase in complication rates across AST categories in the present study suggests that admission AST can serve as a readily available adjunct to clinical warning signs, platelet count and imaging findings.

Serial changes and clinical recovery

Serial evaluation showed significant improvement in hepatic biochemical abnormalities. Mean AST decreased from 160.51 IU/L on day 1 to 117.86 IU/L on day 3 and 67.98 IU/L on day 7, representing a reduction of 92.53 IU/L ($p<0.001$). Mean ALT decreased from 126.13 to 83.93 and 51.42 IU/L, a reduction of 74.71 IU/L ($p<0.001$). Severe AST elevation declined from 15% to 5% and then to 0%, while severe ALT elevation decreased from 6% to 2% and then to 0%. Meanwhile, mean platelet count increased from 75,336 to 113,099 cells/mm³. This parallel decline in aminotransferases and recovery of platelet counts suggests resolution of both hepatic/systemic injury and the critical phase of dengue.

Fernando et al. (2016),[3] who performed daily clinical and biochemical assessment, showed that liver-enzyme changes followed the clinical course and were related to inflammatory markers, viral load and disease severity. Martínez Vega et al. (2016),[4] also documented progressive normalization of liver enzymes, although recovery patterns differed between adults and children. Rao et al. (2020),[7] recommended repeated aminotransferase measurement because a single admission value may not adequately characterize evolving severity. Huy et al. (2022),[9] further showed that the prognostic usefulness of biochemical indicators depended on the day of illness.

CONCLUSION

Serum aminotransferase abnormalities were common among adult dengue patients, with AST and ALT elevations each observed in 66% of cases. AST elevation was generally more pronounced than ALT elevation and showed a significant graded association with severe dengue, thrombocytopenia, bleeding manifestations, plasma leakage, shock, hepatosplenomegaly and organ dysfunction. Serial monitoring demonstrated significant reductions in AST and ALT levels between days 1 and 7, accompanied by recovery of platelet counts and clinical improvement. These findings indicate that admission and serial serum aminotransferase measurements may serve as inexpensive and readily available adjuncts for early risk stratification and monitoring of dengue patients. However, aminotransferases should be interpreted alongside clinical warning signs, haemodynamic status, platelet count, haematocrit and evidence of plasma leakage rather than being used as independent prognostic markers.

Limitations

This study had several limitations. It was a single-centre study involving only 100 hospitalized adults; therefore, its findings may not be generalizable to paediatric patients, outpatients or populations from

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other geographical regions. The observational design established associations but could not confirm a causal relationship between aminotransferase elevation and severe dengue. Patients were enrolled at different stages of illness, which might have influenced admission AST and ALT concentrations. Although individuals with recognized liver disease and selected concurrent infections were excluded, other factors such as subclinical hepatic disease, nutritional status, muscle injury and medication exposure might have affected aminotransferase levels. AST is not liver-specific and may originate from skeletal muscle, cardiac muscle or erythrocytes; consequently, AST elevation could not be attributed entirely to hepatic injury. Creatine kinase and other tissue-injury biomarkers were not routinely measured to differentiate hepatic from extrahepatic AST release. Dengue serotypes, viral load, primary versus secondary infection and quantitative antibody titres were not assessed. Multivariable regression and externally validated ROC-derived cut-offs were not available to establish the independent prognostic performance of AST and ALT. Finally, follow-up was limited to the hospitalization period, preventing assessment of the time required for complete biochemical normalization and any long-term hepatic consequences.

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