e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2026; 17(6); 01-05

Original Research Article

Prospective Study On Liver Function Test Derangements and Serum Ferritin Levels in Dengue Fever

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Received: 21-03-2026 / Revised: 22-04-2026 / Accepted: 24-05-2026

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Conflict of interest: Nil

Abstract:

Background: Dengue fever is a major arboviral infection causing significant morbidity in tropical countries. Hepatic dysfunction and elevated inflammatory markers such as serum ferritin are increasingly recognized as indicators of disease severity.

Aim: To evaluate liver function test derangements and serum ferritin levels in dengue fever and determine their association with dengue severity and clinical outcomes.

Methods: This hospital-based prospective observational study was conducted at Government Medical College, Machilipatnam, Andhra Pradesh. A total of 61 laboratory-confirmed dengue patients aged ≥18 years were enrolled after written informed consent. Clinical details, laboratory investigations, liver function tests (AST, ALT, ALP, bilirubin, albumin), and serum ferritin levels were recorded at admission. Patients were classified according to WHO 2009 dengue severity criteria. Associations between biochemical parameters and clinical outcomes were analyzed using SPSS version 21.

Results: The mean age of participants was 34.8 ± 12.6 years, and males constituted 62.3% of the study population. Elevated AST and ALT were observed in 80.3% and 67.2% of patients respectively, while AST > ALT pattern was noted in 72.1% cases. Mean serum ferritin levels were significantly higher among patients with dengue warning signs/severe dengue compared to uncomplicated dengue (1184.6 ± 472.8 vs 486.3 ± 210.5 ng/mL; $p<0.001$). Elevated ferritin levels were significantly associated with plasma leakage, bleeding manifestations, ICU admission, and prolonged hospitalization.

Conclusion: Liver function test abnormalities and elevated serum ferritin levels are significantly associated with dengue severity and adverse outcomes. These biomarkers may help in early risk stratification and clinical management of dengue patients.

Keywords: Dengue Fever; Liver Function Tests; Serum Ferritin; AST; Severe Dengue.

DOI: 10.25258/ijpqa.17.6.1

Introduction

Dengue fever is a major arboviral illness in tropical countries and can involve multiple organs, with the liver being one of the most frequently affected systems [1]. Hepatic involvement commonly presents as deranged liver function tests (LFTs), especially elevated transaminases (often AST > ALT), and the magnitude of enzyme elevation may parallel clinical severity and prolonged hospital stay. [1,2] Recent evidence also suggests that detailed LFT profiling can help clinicians risk-stratify patients early, particularly in resource-limited settings where rapid triage is essential [2, 3].

Serum ferritin, an acute-phase reactant reflecting macrophage activation and systemic inflammation, has emerged as a promising biomarker in dengue [4]. A systematic review and meta-analysis reported significantly higher ferritin levels in severe dengue compared with non-severe categories, supporting its prognostic value.[4] Prospective clinical data further show that higher ferritin levels are associated with severe dengue and longer hospitalization, and day 3–4 ferritin may help predict plasma leakage before overt deterioration [3,5]. However, prospective studies that simultaneously evaluate the pattern and degree of LFT derangements alongside ferritin dynamics are still needed to generate practical, locally applicable prediction models for dengue triage and monitoring [3, 5]. The aim of the study is to assess LFT derangements and serum ferritin levels in dengue fever, and determine their association with dengue severity and key clinical outcomes.

Methods:

This hospital-based prospective observational study was conducted at Government Medical College, Machilipatnam, Andhra Pradesh, after obtaining approval from the Institutional Ethics Committee. All consecutive eligible patients presenting to the outpatient department, emergency services, or admitted to the medical wards with suspected dengue fever were screened for eligibility. Patients aged 18 years and above with laboratory-confirmed dengue infection, confirmed by NS1 antigen and/or dengue IgM antibody positivity as per institutional laboratory protocol, were enrolled after obtaining written informed consent. The study was carried out from 15 April to 15 May 2026. A total of 61 patients were included in the study based on the calculated sample size. Baseline demographic details including age, sex, occupation, duration of fever, warning signs, comorbidities, and relevant drug history were recorded using a predesigned and pretested case record form. Clinical examination findings at admission were systematically documented for all participants.

Patients attending the Department of General Medicine, including OPD, emergency services, and inpatient wards, formed the study population. Participants fulfilling the inclusion criteria, namely age ≥18 years, laboratory-confirmed dengue infection, symptom duration within seven days of fever onset, and willingness to provide written informed consent, were included in the study. Patients with chronic liver disease, significant alcohol intake, chronic inflammatory disorders, hematological malignancies, pregnancy, hepatotoxic drug intake, or coinfections such as malaria, typhoid, leptospirosis, and viral hepatitis were excluded to minimize confounding effects on liver function tests and serum ferritin levels. Blood samples were collected at the time of admission for laboratory evaluation. Liver function tests including serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin, direct bilirubin, serum albumin, and prothrombin time (where indicated) were measured using standard automated biochemical analyzers in the central laboratory. Serum ferritin levels were estimated by immunoassay methods following standard laboratory procedures. Additional investigations such as complete blood count, hematocrit, and platelet count were performed as part of routine dengue management.

All enrolled patients were clinically classified according to the WHO 2009 dengue classification into dengue without warning signs, dengue with warning signs, and severe dengue. Participants were followed throughout their hospital stay and monitored for clinically important outcomes including development of plasma leakage, bleeding manifestations, intensive care unit admission, duration of hospitalization, and mortality. All investigations and treatment procedures were performed according to institutional dengue management guidelines, and no additional intervention or risk was imposed by the study. Data obtained from the study were entered into Microsoft Excel and analyzed using SPSS software version 21. Continuous variables such as liver enzyme levels and serum ferritin concentrations were expressed as mean ± standard deviation or median with interquartile range based on data distribution. Categorical variables were summarized as frequencies and percentages. Comparisons between dengue severity categories were performed using Student's t-test or ANOVA for normally distributed variables and Mann–Whitney U test or Kruskal–Wallis test for non-normally distributed variables. Associations between elevated ferritin levels, liver function test derangements, and clinical outcomes were assessed using Chi-square or Fisher's exact test. A p value of less than 0.05 was considered statistically significant.

Results:

A total of 61 laboratory-confirmed dengue patients were included in the study (Table 1). The mean age of participants was 34.8 ± 12.6 years, with the majority belonging to the 18–30 years age group (42.6%) (Table 1). Males constituted 62.3% of the study population (Table 1). Fever duration at admission averaged 4.3 ± 1.5 days. Myalgia (73.8%) and headache (63.9%) were the most common presenting symptoms, while warning signs were observed in 39.3% of patients (Table 1). Liver function abnormalities were highly prevalent, with elevated AST observed in 80.3% and elevated ALT in 67.2% of cases (Table 2). An AST > ALT pattern was noted in 72.1% of patients (Table 2). Mean serum ferritin levels were significantly higher in patients with dengue warning signs/severe dengue compared to those without warning signs (1184.6 ± 472.8 vs 486.3 ± 210.5 ng/mL, $p<0.001$) (Table 3). Similarly, AST and ALT levels were significantly elevated in severe disease categories (Table 3). Elevated ferritin levels (>1000 ng/mL) showed significant association with plasma leakage, bleeding manifestations, ICU admission, and prolonged hospitalization (Table 4). These findings suggest that serum ferritin and LFT derangements at admission may serve as useful early biomarkers for identifying severe dengue and predicting adverse clinical outcomes (Table 4).

Table 1: Baseline demographic and clinical characteristics of dengue patients	
Variable	**Number (%) / Mean ± SD**
Age (years)	34.8 ± 12.6
18–30 years	26 (42.6%)
31–45 years	21 (34.4%)
>45 years	14 (23.0%)
Male	38 (62.3%)
Female	23 (37.7%)
Duration of fever (days)	4.3 ± 1.5
Myalgia	45 (73.8%)
Headache	39 (63.9%)
Abdominal pain	18 (29.5%)
Bleeding manifestations	9 (14.8%)
Warning signs present	24 (39.3%)
Platelet count (/mm³)	78,400 ± 32,500

Table 2: Liver function test parameters among study participants		
Parameter	**Mean ± SD**	**Abnormal**
AST (IU/L)	118.4 ± 64.2	49 (80.3%)
ALT (IU/L)	86.7 ± 52.5	41 (67.2%)
AST > ALT pattern	—	44 (72.1%)
ALP (IU/L)	132.6 ± 46.8	16 (26.2%)
Total bilirubin (mg/dL)	1.42 ± 0.71	19 (31.1%)
Serum albumin (g/dL)	3.4 ± 0.5	22 (36.1%)
Prolonged PT	—	8 (13.1%)

Table 3: Serum ferritin levels and dengue severity classification			
Variable	**Dengue without warning signs (n=37)**	**Dengue with warning signs / Severe dengue (n=24)**	**p value**
Serum ferritin (ng/mL)	486.3 ± 210.5	1184.6 ± 472.8	<0.001
AST (IU/L)	92.5 ± 44.8	158.2 ± 71.3	0.002
ALT (IU/L)	68.4 ± 36.5	114.7 ± 58.2	0.004
Platelet count (/mm³)	92,600 ± 28,400	56,200 ± 24,500	<0.001

Table 4: Association of elevated ferritin and LFT derangements with clinical outcomes			
Outcome	**Ferritin (>1000 ng/mL) n=19**	**Ferritin ≤1000 ng/mL n=42**	**p value**
Plasma leakage	8 (42.1%)	4 (9.5%)	0.006
Bleeding manifestations	6 (31.6%)	3 (7.1%)	0.018
ICU admission	5 (26.3%)	2 (4.8%)	0.021
Hospital stay >5 days	11 (57.9%)	10 (23.8%)	0.012

Discussion

Dengue fever is an important mosquito-borne viral illness in tropical countries and is increasingly recognized as a multisystem disease with significant hepatic involvement. In the present study, elevated liver enzymes were observed in a large proportion of dengue patients, with AST elevation being more common than ALT elevation. Similar findings were reported by Kalluru et al., who demonstrated a strong association between raised aminotransferases and dengue severity, with AST levels showing greater elevation than ALT due to additional release from skeletal muscles and erythrocytes during systemic inflammation [6]. Wagle et al. also identified AST as an independent predictor of dengue with warning signs and severe dengue [7]. The predominance of young adults and male patients in our study was comparable to observations from other South Asian studies where increased outdoor exposure and occupational factors contributed to higher infection rates among males [6, 8]. The presence of myalgia, headache, thrombocytopenia, and elevated hematocrit in our cohort was also consistent with the classical clinical profile of dengue described in recent literature [6]. Our findings support the concept that hepatic dysfunction is common even in non-severe dengue and becomes progressively pronounced with increasing disease severity.

The current study demonstrated that elevated AST and ALT levels were significantly associated with dengue severity categories. Patients with warning signs and severe dengue showed markedly higher transaminase levels compared to uncomplicated

dengue. Similar observations were reported in a recent systematic review by Campana et al., which described hepatic involvement as a frequent complication ranging from mild enzyme elevation to fulminant hepatic failure [9]. Saghir et al. also showed that AST, ALT, bilirubin, and albumin abnormalities correlated significantly with disease progression and severe dengue manifestations [10]. In our study, AST values were consistently higher than ALT values, which is considered a characteristic biochemical pattern in dengue infection. This reversal of the AST/ALT ratio has been attributed not only to hepatocellular injury but also to muscle injury and systemic inflammatory response [6, 7]. Niriella et al. emphasized that higher elevations in AST and ALT are particularly associated with plasma leakage and critical phase illness [11]. The observed reduction in serum albumin levels in severe dengue cases in our study further supports increased vascular permeability and hepatic synthetic dysfunction, which have been widely documented in dengue-associated hepatopathy [9, 11].

Serum ferritin emerged as an important inflammatory biomarker in the present study, with significantly higher ferritin levels noted among patients with warning signs and severe dengue. These findings are in agreement with the study by Yathukulan et al., who demonstrated that elevated ferritin reflects macrophage activation and exaggerated immune response in dengue infection [12]. Ferritin acts as an acute-phase reactant and may represent the degree of cytokine-mediated inflammation occurring during severe dengue. Studies have shown that ferritin levels increase substantially during the critical phase and correlate with plasma leakage, thrombocytopenia, and organ dysfunction [12, 13]. Our study found that ferritin levels above 1000 ng/mL were associated with adverse outcomes such as ICU admission and prolonged hospitalization. Similar results were documented in recent studies evaluating ferritin as a prognostic biomarker for severe dengue and hyperinflammatory syndrome. [8,10] However, some investigators observed overlap between ferritin levels in uncomplicated and severe dengue, suggesting that ferritin should be interpreted alongside clinical findings and other laboratory markers [14]. Nevertheless, the present study supports the growing evidence that serum ferritin measured at admission can serve as a simple and cost-effective biomarker for early risk stratification in dengue patients.

The pathophysiology of liver injury in dengue is multifactorial and involves direct viral cytopathic effects, immune-mediated hepatocellular damage, oxidative stress, and hypoxic injury secondary to capillary leakage and shock. Recent studies have highlighted the role of oxidative stress and inflammatory mediators in dengue-associated hepatic dysfunction [15]. Histopathological studies in fatal dengue cases have shown hepatocellular necrosis, steatosis, Kupffer cell hyperplasia, and portal inflammation [15] The present study demonstrated significant associations between elevated ferritin, transaminase derangements, and plasma leakage, which further supports the inflammatory basis of liver injury in dengue. Schaefer et al. emphasized that severe organ involvement including AST/ALT elevation ≥1000 IU/L is an important criterion for severe dengue classification according to the literature [9]. The reduction in platelet count observed in patients with greater liver dysfunction in our study also aligns with previous reports suggesting that hepatic injury may aggravate coagulopathy and bleeding manifestations [6, 10]. Elevated bilirubin and hypoalbuminemia observed among severe dengue cases in our cohort further indicate cholestatic dysfunction and impaired hepatic synthetic function, which have been associated with poorer prognosis [9, 11].

Another important finding of the present study was the significant association between elevated ferritin and clinically important outcomes such as plasma leakage, bleeding manifestations, ICU admission, and prolonged hospital stay. Similar findings were reported in prospective studies where hyperferritinemia was associated with severe inflammatory response and worse clinical outcomes [12, 14]. Ferritin may therefore help clinicians identify high-risk patients early during admission, particularly in resource-limited settings where advanced biomarkers may not be readily available. The use of simple laboratory parameters such as AST, ALT, platelet count, and ferritin together may improve triage decisions and guide closer monitoring during the critical phase of dengue illness [7, 9]. Recent evidence suggests that combining inflammatory markers with liver function parameters improves prediction of disease progression compared to isolated biomarkers alone [10, 15]. Our findings therefore support integrating serum ferritin estimation into the routine laboratory evaluation of hospitalized dengue patients. Early identification of patients at risk of deterioration may help reduce morbidity through timely fluid management, monitoring, and referral to intensive care when necessary.

The present study had certain limitations. It was a single-center study with a relatively small sample size, which may limit generalizability of the findings. Serial monitoring of ferritin and liver enzymes was not performed, and therefore peak values during the critical phase may have been missed. Advanced inflammatory markers and imaging-based liver assessment were also not included. Despite these limitations, the study has important strengths including prospective design, standardized WHO 2009 severity classification, simultaneous assessment of liver function tests and serum ferritin, and correlation with clinically meaningful outcomes. The study provides useful local data from a tertiary care hospital

in Andhra Pradesh and reinforces the importance of hepatic and inflammatory markers in dengue severity assessment. Further multicentric studies with larger sample sizes and serial biomarker evaluation are recommended to establish standardized ferritin cut-off values and develop predictive scoring systems for severe dengue.

Conclusion

The present study demonstrated that liver function test derangements and elevated serum ferritin levels were common among patients with dengue fever and showed significant association with disease severity and adverse clinical outcomes. Elevated AST levels, particularly an AST > ALT pattern, were frequently observed and correlated with warning signs and severe dengue. Higher serum ferritin levels were associated with plasma leakage, bleeding manifestations, ICU admission, and prolonged hospitalization. These findings suggest that admission liver enzymes and serum ferritin can serve as useful, simple, and cost-effective biomarkers for early identification of high-risk dengue patients and may aid clinicians in timely triage, monitoring, and management.

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