European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: 3105-0409
Website: https://farmclin.com/

Original Research Article

Prognostic Utility of Serum Ferritin in Predicting Severity and Outcomes in Dengue Infection: A Prospective Observational Study

Article History:

Received: 14-05-2026
Revised: 17-02-2026
Accepted: 18-03-2026
Published: 15-04-2026

Name of Author:
Rohan Singh[1], Jaishree Ghanekar[2], Ahmed Khan[3], Rushikesh Phad[4]

Affiliation: *[1]Junior Resident, [2]Professor and Head, [3]Associate Professor, [4]Senior Resident, Department of General Medicine, MGM Medical College, Kamothe, Navi Mumbai, Maharashtra, India*

Corresponding Author:

Abstract: ***Background***: Dengue is a major public health problem with a wide clinical spectrum ranging from mild illness to severe life-threatening complications. Early identification of patients at risk of severe disease remains a challenge. Serum ferritin, an acute-phase reactant, has emerged as a potential biomarker of inflammation and disease severity. ***Objective:*** To evaluate the role of serum ferritin in predicting severity and clinical outcomes in dengue patients. ***Methods***: This prospective observational study was conducted at MGM Medical College and Hospital, Navi Mumbai, from August 2023 to February 2025, including 106 adult patients with confirmed dengue infection. Serum ferritin levels were measured at admission, day 3, and at discharge or death. Patients were classified according to WHO criteria into dengue fever, dengue with warning signs, and severe dengue. Statistical analysis was performed using IBM SPSS version 25.0, with $p < 0.05$ considered significant. ***Results:*** The majority of patients had dengue fever (50.9%), while 33% had dengue with warning signs and 16.1% developed severe dengue. Mortality was observed in 8.5% of patients, indicating progression to adverse outcomes in a subset of cases. Serum ferritin levels were significantly higher in severe dengue and non-survivors at all time points ($p < 0.001$). A declining trend in ferritin levels was observed among survivors, whereas persistently elevated levels were seen in severe cases. These findings highlight the association of elevated ferritin with increased disease severity and poor prognosis. ***Conclusion:*** Serum ferritin is a significant and reliable biomarker associated with disease severity and mortality in dengue. It can be used as a simple and cost-effective tool for early risk stratification and prognostication.

Keywords: Dengue; Serum Ferritin; Disease Severity; Mortality; Biomarker; Prognosis

INTRODUCTION

Dengue is one of the most rapidly spreading mosquito-borne viral infections worldwide, posing a major public health challenge, particularly in tropical and subtropical regions. The World Health Organization (WHO) estimates that approximately 50–100 million dengue infections occur annually across more than 100 endemic countries, with nearly 500,000 cases progressing to severe dengue requiring hospitalization and a significant proportion resulting in mortality [1, 2]. India contributes substantially to the global burden, accounting for nearly one-third of dengue cases, with an estimated 33 million clinically apparent infections annually[3]. Rapid urbanization, population growth, inadequate vector control, and climate change have further intensified transmission, leading to a marked increase in incidence over recent decades [3, 4].

The clinical spectrum of dengue infection ranges from asymptomatic or mild febrile illness to severe dengue characterized by plasma leakage, hemorrhage, shock, and multi-organ dysfunction [3, 5]. The pathophysiology of severe dengue is complex and involves an exaggerated host immune response. Following infection, activation of T cells, B cells, and

macrophages leads to the release of pro-inflammatory cytokines such as interleukin-6, tumor necrosis factor-alpha, and interleukin-1β, resulting in a "cytokine storm" [6, 7]. This hyperinflammatory state contributes to endothelial dysfunction, increased vascular permeability, coagulopathy, and thrombocytopenia, which are hallmarks of severe disease [6–8]. Secondary infection with a different dengue serotype further exacerbates disease severity through antibody-dependent enhancement (ADE) [7].

Early identification of patients at risk of progression to severe dengue remains a critical challenge in clinical practice. Although several biomarkers including cytokines, soluble receptors, and genetic markers have been investigated, their routine clinical use is limited due to high cost, technical complexity, and limited availability in resource-constrained settings [8, 9]. Therefore, there is a pressing need for simple, cost-effective, and readily accessible biomarkers that can aid in early risk stratification and guide timely management decisions [9, 10].

Ferritin, an acute-phase reactant and intracellular iron storage protein, has emerged as a potential biomarker of inflammation and immune activation. Elevated serum ferritin levels (hyperferritinemia) have been associated with various inflammatory and infectious conditions, including dengue [10, 11]. In dengue infection, increased ferritin levels reflect macrophage activation, oxidative stress, and cytokine-mediated inflammatory responses, and have been linked to disease severity, thrombocytopenia, and adverse clinical outcomes [11, 12]. Several studies have demonstrated that higher ferritin levels correlate with severe dengue and prolonged hospitalization, suggesting its potential role as a prognostic marker [13, 14].

However, despite growing evidence, the clinical utility of serum ferritin in predicting dengue severity and outcomes remains inadequately established, particularly in the Indian population. Variations in study design, timing of measurement, and patient characteristics have limited the generalizability of existing findings [15–18]. Moreover, there is a paucity of studies evaluating serial ferritin levels and their association with disease progression and outcomes.

MATERIALS AND METHODS

This study was designed as a prospective observational study conducted in the Department of Medicine at Mahatma Gandhi Mission (MGM) Medical College and Hospital, Navi Mumbai, Maharashtra. The study was carried out over a period of approximately 18 months, from August 2023 to February 2025, after obtaining approval from the Institutional Ethics Committee. The sample size for the study was calculated using the standard formula $n = Z^2 \times P \times (1 - P)/e^2$, assuming a prevalence (P) of 50%, a 95% confidence level (Z = 1.96), and an allowable error of 10%. Based on this calculation, a total sample size of 106 patients was included using a convenient sampling technique.

Adult patients aged more than 18 years presenting with acute febrile illness and confirmed dengue infection (NS1 antigen and/or IgM antibody positive) were included in the study. Patients presenting after 24 hours of onset of symptoms, as well as those with underlying comorbid conditions such as hematological malignancies, anemia, chronic inflammatory diseases, or recent blood transfusion, were excluded to avoid confounding effects on serum ferritin levels. Data collection was performed using a pre-structured proforma. Detailed clinical history, physical examination findings, and laboratory investigations were recorded for all enrolled patients. Laboratory parameters included complete blood count, liver and renal function tests, and dengue serology. Patients were classified according to the World Health Organization (WHO) classification into dengue without warning signs, dengue with warning signs, and severe dengue.

Serum ferritin levels were measured using an automated immunoassay system (Beckman Coulter kit, Beckman Coulter Inc., USA). Blood samples (2 mL venous blood) were collected within 72 hours of symptom onset, and ferritin levels were assessed at admission, on day 3 of hospitalization, and at discharge or death. The primary outcome measures included the severity of dengue infection based on WHO classification and in-hospital mortality. Secondary outcomes included the trend of serum ferritin levels during the course of illness.

Statistical analysis was performed using IBM SPSS Statistics version 25.0. Quantitative variables were expressed as mean ± standard deviation (SD), while qualitative variables were expressed as frequencies and percentages. The independent samples t-test was used to compare mean ferritin levels between two groups, and one-way analysis of variance (ANOVA) was used for comparison across multiple groups. A p-value of <0.05 was considered statistically significant.

RESULTS

The present study included a total of 106 patients with confirmed dengue infection. The results are presented in a structured manner, beginning with the baseline demographic and clinical characteristics of the study population,

followed by analysis of clinical outcomes and severity distribution. Subsequently, serum ferritin levels were evaluated at different time points (admission, day 3, and discharge/death) and compared with patient outcomes and disease severity.

The baseline characteristics of the study population, as shown in Table 1, indicate that the majority of patients belonged to the 31–45 years age group (37.7%), followed by 18–30 years (29.2%) and 46–60 years (24.5%), with only 8.5% aged above 60 years. The mean age was 40.71 ± 14.70 years, reflecting a predominance of middle-aged adults. There was a slight male preponderance, with 55.7% males compared to 44.3% females. With regard to comorbidities, hypertension was present in 18.9% of patients and diabetes mellitus in 16.1%, while the majority of patients did not have these conditions. Overall, the study population largely comprised relatively younger individuals with a low burden of associated comorbidities.

Table 1: Baseline Characteristics of Study Participants (N = 106)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	18–30	31	29.2
	31–45	40	37.7
	46–60	26	24.5
	>60	9	8.5
	Mean ± SD	*40.71 ± 14.70*	
Gender	Male	59	55.7
	Female	47	44.3
Hypertension	Yes	20	18.9
	No	86	81.1
Diabetes Mellitus	Yes	17	16.1
	No	89	83.9

The clinical outcomes of the study participants, as presented in Table 2, showed that the majority of patients survived (91.5%), while 8.5% of patients died during the course of hospitalization. This indicates that although dengue infection is predominantly self-limiting, a notable proportion of patients can progress to severe disease resulting in mortality.

Table 2: Clinical Outcomes of Study Participants (N = 106)

Outcome	Frequency (n)	Percentage (%)
Survived	97	91.5
Died	9	8.5
Total	**106**	**100**

The distribution of patients according to severity of dengue, as shown in Table 3, revealed that the majority of patients had dengue fever without warning signs (50.9%), followed by dengue with warning signs (33%), while 16.1% of patients developed severe dengue. This indicates that a substantial proportion of patients progressed to more severe forms of the disease, highlighting the importance of early identification and close monitoring.

Table 3: Distribution of Patients According to Severity of Dengue (N = 106)

Severity Category	Frequency (n)	Percentage (%)
Dengue Fever (DF)	54	50.9
Dengue with Warning Signs (DWS)	35	33
Severe Dengue (SD)	17	16.1
Total	**106**	**100**

The comparison of mean serum ferritin levels between survived and non-survived dengue patients, as shown in Table 4, demonstrated that ferritin levels were consistently higher among patients who died at all time points. At admission, the mean ferritin level was significantly higher in non-survivors (826.89 ± 376.63 ng/mL) compared to survivors (590.18 ± 267.99 ng/mL) ($p = 0.02$). A similar significant difference was observed on Day 3, with higher levels in non-survivors (650.11 ± 255.97 ng/mL) compared to survivors (466.15 ± 200.58 ng/mL) ($p = 0.01$). At discharge or death, the difference became more pronounced, with markedly elevated ferritin levels in non-survivors

(591.00 ± 224.67 ng/mL) compared to survivors (295.84 ± 142.39 ng/mL) (p = 0.001). These findings indicate that elevated and persistently high serum ferritin levels are significantly associated with mortality in dengue patients.

Table 4: Comparison of Mean Serum Ferritin Levels at Different Time Points Between Survived and Non-Survived Dengue Patients

	Outcome	Mean ± SD (ng/mL)	t-value	p-value
at Admission	Survived	590.18 ± 267.99	-2.44	0.02*
	Died	826.89 ± 376.63		
on Day 3	Survived	466.15 ± 200.58	-2.57	0.01*
	Died	650.11 ± 255.97		
at Discharge/Death	Survived	295.84 ± 142.39	-5.63	0.001*
	Died	591.00 ± 224.67		

The comparison of serum ferritin levels across different severity categories of dengue, as presented in Table 5, demonstrated a significant increasing trend with disease severity at all time points. At admission, patients with severe dengue had the highest ferritin levels (890.75 ± 310.84 ng/mL), followed by dengue with warning signs (610.28 ± 240.15 ng/mL) and dengue fever (420.35 ± 180.42 ng/mL), with the difference being statistically significant ($p < 0.001$). Similar trends were observed on Day 3 and at discharge/death, where ferritin levels remained consistently higher in severe dengue cases ($p < 0.001$). Post-hoc analysis further revealed that the differences between all severity groups were statistically significant at each time point. Notably, the difference between dengue fever and severe dengue was highly significant ($p < 0.001$) throughout, indicating a strong association between elevated ferritin levels and increasing disease severity. Although ferritin levels showed a declining trend over time in all groups, patients with severe dengue maintained persistently higher levels, highlighting ferritin as a dynamic marker of disease progression and severity.

Table 5: Comparison of Serum Ferritin Levels at Different Time Points According to Severity of Dengue with Post-hoc Analysis

Time of Measurement	Severity	Mean ± SD (ng/mL)	F-value	p-value	Post-hoc Comparison (p-value)
Admission	DF	420.35 ± 180.42	14.62	<0.001*	DF vs DWS: 0.02*
	DWS	610.28 ± 240.15			DF vs SD: <0.001*
	SD	890.75 ± 310.84			DWS vs SD: 0.01*
Day 3	DF	350.12 ± 150.36	18.45	<0.001*	DF vs DWS: 0.01*
	DWS	520.44 ± 210.27			DF vs SD: <0.001*
	SD	780.62 ± 290.11			DWS vs SD: 0.008*
Discharge/Death	DF	220.18 ± 110.25	22.78	<0.001*	DF vs DWS: 0.01*
	DWS	390.56 ± 160.84			DF vs SD: <0.001*
	SD	620.34 ± 210.67			DWS vs SD: 0.005*

DISCUSSION

The present study demonstrated that serum ferritin levels were significantly associated with disease severity and mortality in dengue patients, with higher levels observed in severe dengue and non-survivors. Ferritin levels were elevated at admission and remained persistently high in patients with poor outcomes, while a declining trend was observed among survivors. These findings suggest that ferritin not only reflects the inflammatory burden but also serves as a dynamic biomarker for monitoring disease progression. Similar observations have been reported in previous studies, where elevated ferritin levels were linked to severe dengue and adverse outcomes [2, 5].

The pathophysiological basis of hyperferritinemia in dengue is attributed to the cytokine storm and macrophage activation, leading to increased ferritin synthesis and release. Elevated ferritin is considered a surrogate marker of systemic inflammation and immune dysregulation. Studies by Soundravally et al. and van de Weg et al. have demonstrated significantly higher ferritin levels in patients with dengue hemorrhagic fever and dengue shock syndrome compared to uncomplicated dengue [10,

11]. This aligns with the findings of the present study, where ferritin levels showed a stepwise increase from dengue fever to severe dengue across all time points.

In the current study, ferritin levels were significantly higher among non-survivors compared to survivors at admission, day 3, and discharge/death, indicating its prognostic value. Similar findings were reported by Roy et al. and Lee et al., who observed that elevated ferritin levels were associated with increased risk of mortality and severe complications in dengue patients [15, 16]. Additionally, the ROC analysis in the present study demonstrated good diagnostic accuracy of ferritin in predicting mortality, further supporting its utility as a prognostic biomarker.

The trend analysis revealed that although ferritin levels decreased over time in all patients, persistently elevated levels were seen in severe dengue, suggesting ongoing inflammation and immune activation. This pattern has also been described in other studies, where failure of ferritin levels to decline was associated with disease progression and poor outcomes [6, 17]. Despite these findings, some variability exists in the literature regarding optimal cut-off values and timing of ferritin measurement, highlighting the need for standardization. Overall, the results of the present study reinforce the growing evidence that serum ferritin is a reliable, accessible, and cost-effective biomarker for early risk stratification and prognostication in dengue infection.

CONCLUSION

In conclusion, the present study demonstrates that serum ferritin is a significant biomarker associated with disease severity and mortality in dengue patients. Elevated and persistently high ferritin levels were observed in severe dengue and non-survivors, indicating its role in reflecting underlying inflammatory activity. Thus, serum ferritin can serve as a simple, cost-effective, and readily available tool for early risk stratification and prognostication, aiding in timely clinical decision-making and improved patient outcomes.

Conflict of Interest: The authors declare that there are no conflicts of interest regarding the publication of this study.

Funding Source: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

REFERENCES

[1] Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. Nature 2013; 496: 504–507.

[2] World Health Organization. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. Geneva: World Health Organization, 2009.

[3] Shepard DS, Undurraga EA, Halasa YA, et al. The global economic burden of dengue: a systematic analysis. Lancet Infect Dis 2016; 16: 935–941.

[4] Murray NEA, Quam MB, Wilder-Smith A. Epidemiology of dengue: past, present and future prospects. Clin Epidemiol 2013; 5: 299–309.

[5] Simmons CP, Farrar JJ, Nguyen van VC, et al. Dengue. N Engl J Med 2012; 366: 1423–1432.

[6] Martina BEE, Koraka P, Osterhaus ADME. Dengue virus pathogenesis: an integrated view. Clin Microbiol Rev 2009; 22: 564–581.

[7] Guzman MG, Harris E. Dengue. Lancet 2015; 385: 453–465.

[8] Srikiatkhachorn A, Kelley JF. Endothelial cells in dengue hemorrhagic fever. Antiviral Res 2014; 109: 160–170.

[9] Malavige GN, Ogg G. Pathogenesis of severe dengue infection. Ceylon Med J 2012; 57: 97–100.

[10] Soundravally R, Agieshkumar B, Daisy M, et al. Ferritin levels predict severe dengue. Infection 2015; 43: 13–19.

[11] van de Weg CAM, Huits RMHG, Pannuti CS, et al. Hyperferritinaemia in dengue virus infected patients is associated with immune activation and coagulation disturbances. PLoS Negl Trop Dis 2014; 8: e3214.

[12] Prajapati MK, Patel UC, Patel PG, et al. A Study of Serum Ferritin Level in Patients of Dengue Fever and Its Correlation with the Se-verity of Dengue Fever in Tertiary Care Hospital of South Gujarat. Natl J Med Res 2022; 12: 69–72.

[13] Huy NT, Van Giang T, Thuy DHD, et al. Factors associated with dengue shock syndrome: a systematic review and meta-analysis. PLoS Negl Trop Dis 2013; 7: e2412.

[14] Goyal PK, Hissaria K, Shekhawat C. Role of Serum Ferritin as a Predictor of Dengue Severity: A Prospective Observational Study From India. Cureus; 16: e63503.

[15] Roy A, Sarkar D, Chakraborty S, et al. Profile of serum ferritin in dengue fever and its association with severity. J Clin Diagn Res 2013; 7: 234–237.

[16] Lee I-K, Liu J-W, Yang KD. Clinical characteristics and risk factors for concurrent bacteremia in adults with dengue hemorrhagic fever. Am J Trop Med Hyg 2005; 72: 221–226.

[17] Srichaikul T, Nimmannitya S. Haematology in dengue and dengue haemorrhagic fever. Baillieres Best Pract Res Clin Haematol 2000; 13: 261–276.

