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To Study the Correlation Between Serum Ferritin Levels and Severity of Dengue Fever in Patients Above 18 Years

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Abstract

Introduction: Dengue infection is increasing with rapid urbanization in India. Severe dengue reflects a dysregulated host response with capillary leak, coagulopathy, and organ dysfunction.

Aims and objectives:

Aim

- To evaluate the association between serum ferritin levels and clinical severity of dengue fever in adults

Objectives

1. To compare serum ferritin levels among WHO 2009 severity categories (A, B, C).
2. To determine the predictive value of Day-1 and Day-4 ferritin levels for severe dengue.
3. To derive optimal ferritin cut-off values using ROC analysis.
4. To assess the correlation of ferritin with platelet count, hematocrit, and liver enzymes.

Material and method

Study Design: The study was designed as a prospective observational study.

Study Place: The current study was carried out at Shri Venkateshwara University's General Medicine Department in Gajraula, Uttar Pradesh.

Study Period: The study was conducted eighteen months.

Study Participants: The study included patients diagnosed with acute febrile illness and laboratory-confirmed dengue infection (NS1 antigen and/or IgM antibody positive).

Sample Size: Total Sample Size is 60.

Result: The present study included 60 patients with confirmed dengue infection, the mean age (±SD) was 31.4 ± 9.2 years in WHO group A (n = 20), 36.8 ± 11.5 years in group B (n = 28), and 41.3 ± 13.1 years in group C (n = 12) (p = 0.051).

Discussion: Dengue fever continues to pose a substantial clinical and public health challenge due to its unpredictable progression and the potential for rapid deterioration into severe forms characterized by plasma leakage, hemorrhage, and organ dysfunction.

Keywords: Coagulopathy, Cytopenias, Dengue, Hemophagocytosis, Ferritin, Serotype.

Introduction

Dengue is an arboviral illness transmitted by Aedes mosquitoes and is clinically stratified by the WHO 2009 framework into WHO 2009 Category A (without warning signs), Category B (with warning signs), and Category C (severe dengue); this stratification guides triage, monitoring, and escalation of care in adult services [1].

Accurate confirmation during the acute phase uses NS1 antigen and/or IgM assays, which support timely case identification within the inclusion criteria relevant to this protocol [3]. Severe dengue reflects a dysregulated host response with capillary leak, coagulopathy, and organ dysfunction, demanding early indicators that anticipate deterioration before overt decompensation[4]. Hyperinflammatory phenotypes with hemophagocytosis appear within the dengue spectrum and indicate macrophage activation, cytopenias, and multiorgan involvement [6]. In this context, ferritin Introduction 2 gains attention as a practical, widely available signal of systemic inflammation relevant to admission triage in adult care[9]. Recent clinical analyses of early markers characterize phases when deterioration emerges, aligning with the global need for admission-ready indicators that complement standard monitoring in busy hospitals[10]. Work across South and Southeast Asia evaluates ferritin as a diagnostic adjunct in acute dengue cohorts, reflecting the sustained regional burden and the operational need for scalable biomarkers[11]. First contact ferritin associates with subsequent severe thrombocytopenia, mirroring patterns seen during peak seasons when rapid triage influences outcomes[13]. Contemporary reviews continue to position ferritin as a promising triage tool pending standardization of timing and cut-offs in adult populations typical of Indian services[18]. Trace-metal and iron-handling disturbances in dengue suggest biological routes for ferritin up-regulation, yet they also introduce interpretive complexity when hepatic injury coexists[19]. Correlation between ferritin and hepatic injury markers indicates that ferritin may integrate systemic inflammation with organ involvement, necessitating multivariable interpretation with AST/ALT in adult cohorts[21]. Serotype-related clinical differences persist; although ferritin is not serotype-specific, a unified inflammatory endpoint strengthens its appeal, pending local calibration[24].

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Sample Size: Total Sample Size is 60.

Inclusion Criteria

1. Any patient older than 18 years
2. History of fever with a dengue-positive profile (NS1 antigen and IgM antibody positive) was taken into consideration.

Exclusion Criteria

All cases that involve

1. Anemia
2. Chronic inflammatory disease
3. Recent blood transfusion

Statistical Analysis

- Data were analyzed using SPSS version 26.0. Normality of continuous variables was assessed using the Shapiro–Wilk test. Continuous variables were expressed as mean ± standard deviation or median (interquartile range), and categorical variables as frequency and percentage.
- Serum ferritin levels across WHO 2009 severity categories (Category A/B/C) were compared using one-way ANOVA for normally distributed data and the Kruskal–Wallis test for non-normal distributions, with Tukey or Dunn post-hoc tests using Bonferroni correction.
- Receiver operating characteristic (ROC) curve analysis was performed to determine the predictive performance of Day-1 and Day-4 ferritin for identifying Category C (severe dengue). The area under the curve (AUC) and optimal ROC-derived cut-off values were calculated. A two-sided p-value <0.05 was considered statistically significant.

Result

The present prospective observational study was conducted to evaluate the correlation between serum ferritin levels and the severity of dengue fever in adult patients above 18 years of age. A total of 68 patients with suspected dengue fever were assessed for eligibility. Of these, 8 patients were excluded due to predefined exclusion criteria, including anemia in 3 patients, chronic inflammatory disease in 2 patients, and recent blood transfusion in 3 patients. Finally, 60 laboratory-confirmed dengue patients were included and analyzed in the study.

Table 1: Sociodemographic Profile—Age & Sex by WHO-2009 Severity

Variable	A (n=20)	B (n=28)	C (n=12)	Test / effect size
Age, years (mean ± SD)	31.4 ± 9.2	36.8 ± 11.5	41.3 ± 13.1	ANOVA, $F(2,57)=3.15$, $p=0.051$, $n^2 = 0.099$
Male, n (%)	13	18	8	$\chi^2(2)=0.02$, $p=0.990$, Cramér's V=0.019.
Female, n (%)	7	10	4	

In this cohort (N = 60), the mean age (±SD) was 31.4 ± 9.2 years in WHO group A (n = 20), 36.8 ± 11.5 years in group B (n = 28), and 41.3 ± 13.1 years in group C (n = 12) (p = 0.051). Sex distribution was: group A— 13/20 males (65.0%) and 7/20 females (35.0%); group B—18/28 males (64.3%) and 10/28 females (35.7%); group C—8/12 males (66.7%) and 4/12 females (33.3%) (p = 0.990).

Figure 1: Sociodemographic Profile—Age & Sex by WHO-2009 Severity

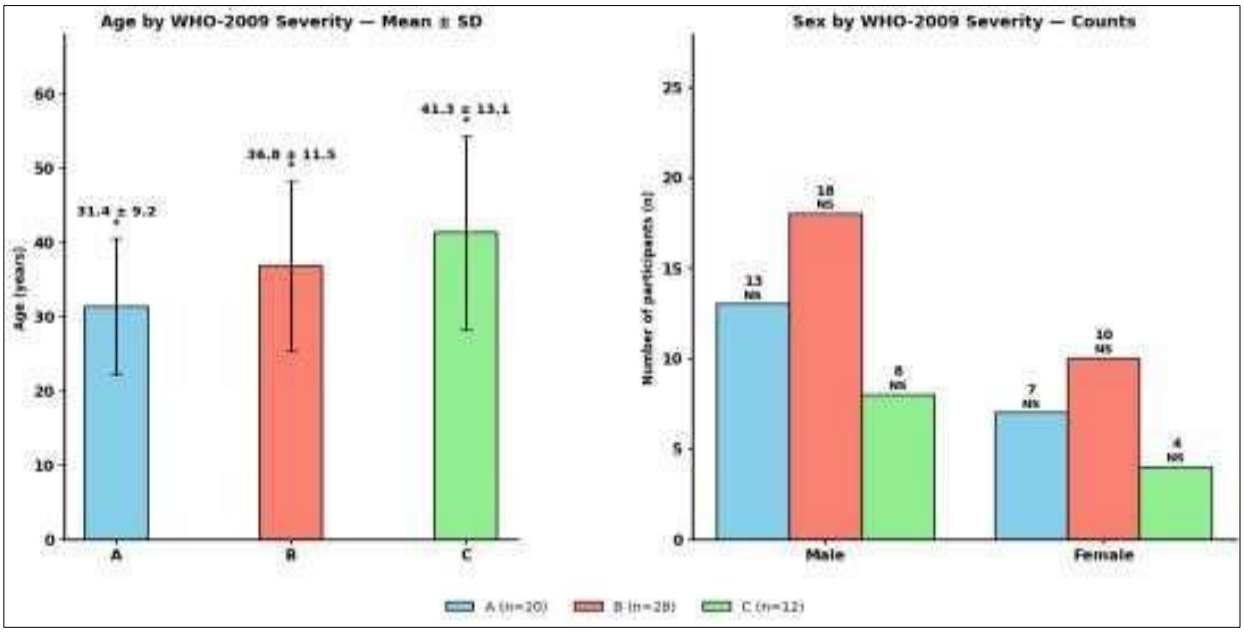


Table 2: Education Distribution by Severity

Education	A	B	C	Total	p-value (χ^2)
Illiterate	1	3	1	5	$\chi^2(8)=2.66$, p=0.954, Cramér's V=0.14 9.
Primary	3	6	3	12	
Secondary	7	9	3	19	
Higher secondary	5	6	2	13	
Graduate+	4	4	3	11	

Among the study participants (N = 60), educational status showed that 5 were illiterate, 12 had primary education, 19 had completed secondary education, 13 had higher secondary education, and 11 were graduates or above; distribution across WHO categories A (n = 20), B (n = 28), and C (n = 12) yielded a chi-square p-value of 0.954.

Figure 2: Education Distribution by Severity

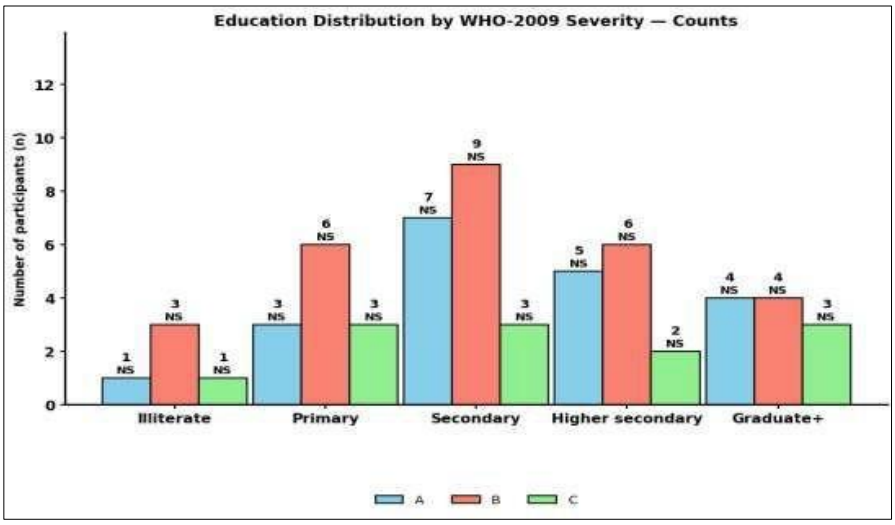


Table 3: Socioeconomic status (Modified Kuppuswamy) by WHO 2009 severity category (N=60)

Kuppuswamy class	Category A (n=20)	Category B (n=28)	Category C (n=12)	Total	p-value (χ^2)
I Upper	1 (5.0)	2 (7.1)	0 (0.0)	3	$\chi^2(8)=1.39$, p=0.994, Cramér's V=0.108.
II Upper-middle	4 (20.0)	6 (21.4)	2 (16.7)	12	
III Lower-middle	7 (35.0)	9 (32.1)	5 (41.7)	21	
IV Upper-lower	6 (30.0)	8 (28.6)	4 (33.3)	18	
V Lower	2 (10.0)	3 (10.7)	1 (8.3)	6	

Socioeconomic assessment using the Kuppuswamy scale showed 3 participants in class I, 12 in class II, 21 in class III, 18 in class IV, and 6 in class V, distributed across WHO groups A (n = 20), B (n = 28), and C (n = 12), with a chi-square p-value of 0.994.

Figure 3: Socioeconomic status (Modified Kuppuswamy) by WHO 2009 severity category (N=60)

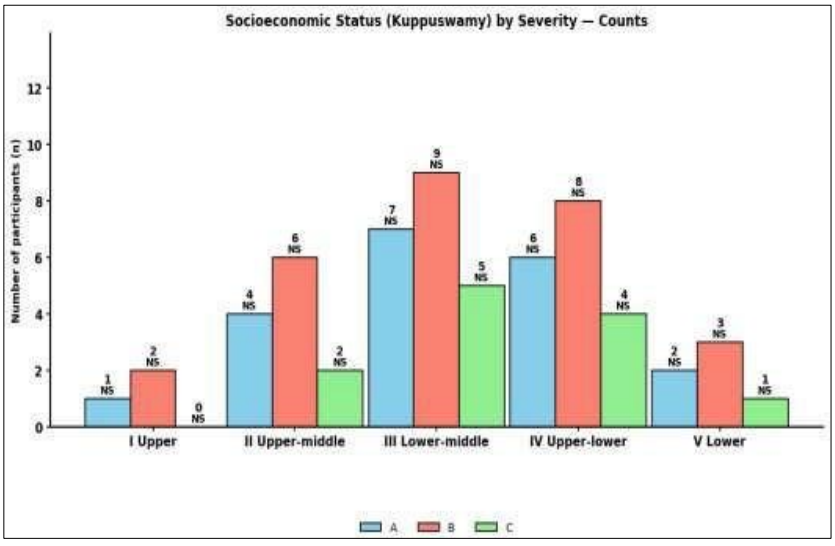


Table 4: Lifestyle factors by WHO 2009 severity category (N=60)

Variable	Category A (n=20)	Category B (n=28)	Category C (n=12)	χ^2 (df)	p	Cramér's V
Alcohol use	3 (15.0)	7 (25.0)	4 (33.3)	1.49 (2)	0.475	0.158
Current smoking	2 (10.0)	6 (21.4)	4 (33.3)	2.62 (2)	0.270	0.209
Vegetarian diet	12 (60.0)	16 (57.1)	8 (66.7)	0.32 (2)	0.853	0.073

Lifestyle assessment indicated 14 participants reported alcohol use, 12 were current smokers, and 36 followed a vegetarian diet, distributed across WHO categories A (n = 20), B (n = 28), and C (n = 12), with p-values of 0.475, 0.270, and 0.853 respectively.

Figure 4: Lifestyle Factors by Severity

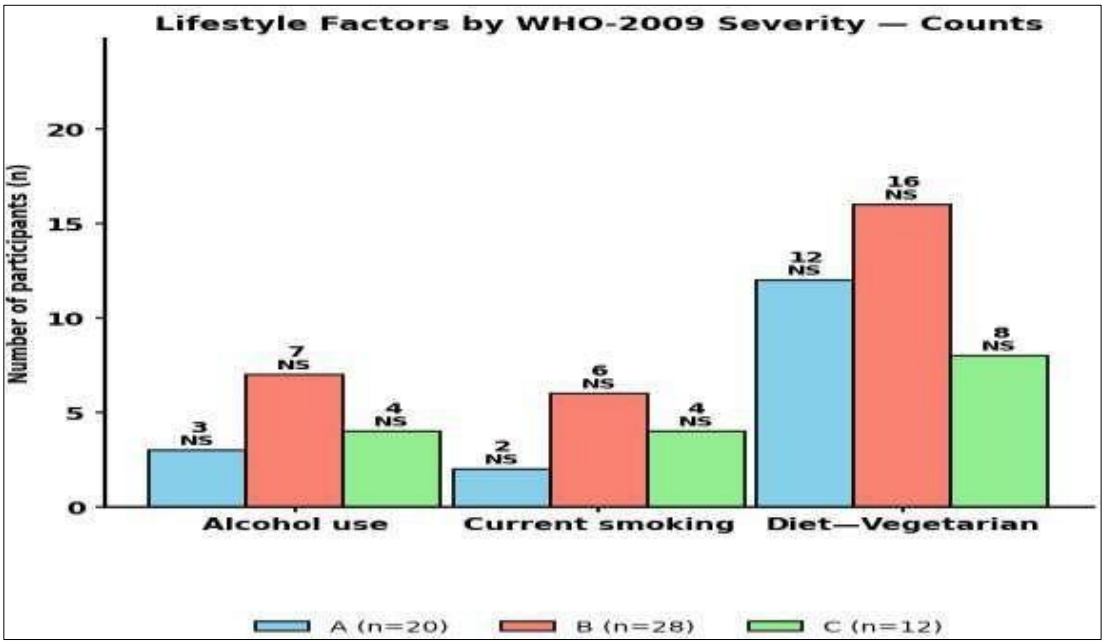


Table 5: Serum Electrolytes by Severity (mean ± SD)

Parameter	A (n=2 0)	B (n=2 8)	C (n=1 2)	F(df1,df2)	p	η^2
Sodium (mmol/L)	134.8±3.2*	132.9±3.6*	130.4±4.1*	5.39(2,57)	0.007	0.159
Potassium(mmol/L)	4.02±0.42*	3.82±0.50*	3.61±0.58*	2.54(2,57)	0.088	0.082

Mean serum sodium decreased progressively with increasing WHO 2009 severity (Category A: 134.8 ± 3.2 mmol/L; Category B: 132.9 ± 3.6 mmol/L; Category C: 130.4 ± 4.1 mmol/L) and differed significantly across categories ($F(2,57)=5.39$, $p=0.007$; $\eta^2=0.159$). Serum potassium also showed a downward trend (4.02 ± 0.42 vs 3.82 ± 0.50 vs 3.61 ± 0.58 mmol/L), but the overall difference was not statistically significant ($F(2,57)=2.54$, $p=0.088$; $\eta^2=0.082$).

Figure 5: Serum Electrolytes by Severity (mean ± SD)

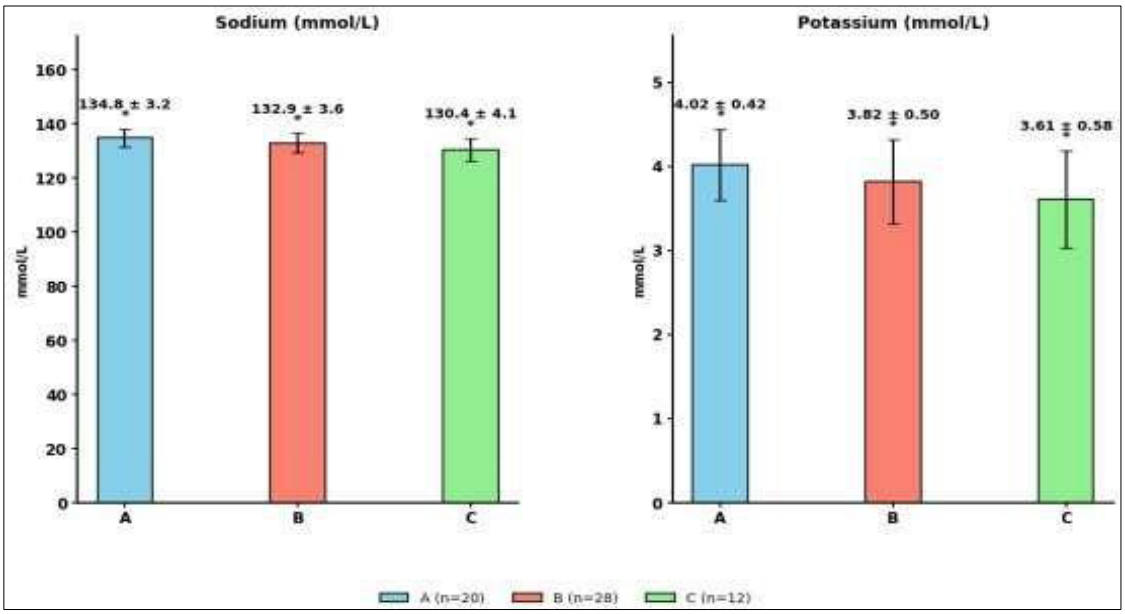


Table 6: Dengue Serology Patterns by Severity

Pattern	A	B	C	Total	p-value (χ^2)
NS1 only	14	14	4	32	$\chi^2(4)=5.64$, p=0.227, Cramér's V=0.217.
IgM only	4	10	4	18	
NS1 + IgM	2	4	4	10	

Dengue serology revealed 32 patients positive for NS1 only, 18 for IgM only, and 10 with both NS1 and IgM positivity, across WHO categories A (n = 20), B (n = 28), and C (n = 12), with a chi-square p-value of 0.227.

Figure 6: Dengue Serology Patterns by Severity

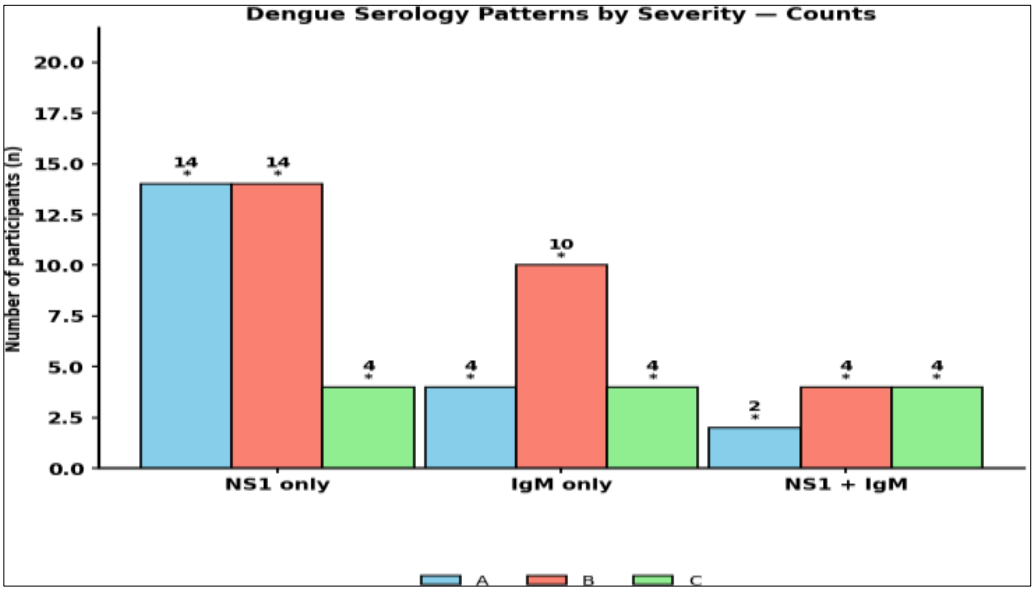


Table 7: ROC—Day-1 and 4 Ferritin Predicting Severe Dengue (C)

AUC (95% CI)	Optimal cut-off (ng/mL)	Sensitivity	Specificity	p-value
0.86 (0.76–0.95)	3,200	0.83	0.78	0.001
0.90 (0.82–0.98)	4,500	0.92	0.82	0.001

ROC analysis showed day-1 ferritin with an AUC of 0.86 (95% CI: 0.76–0.95) at an optimal cut-off of 3,200 ng/mL, yielding sensitivity 0.83 and specificity 0.78 (p = 0.001). Day-4 ferritin demonstrated an AUC of 0.90 (95% CI: 0.82–0.98) with a cut-off of 4,500 ng/mL, sensitivity 0.92, and specificity 0.82 (p = 0.001).

Figure 7: ROC—Day-1 and 4 Ferritin Predicting Severe Dengue (C)

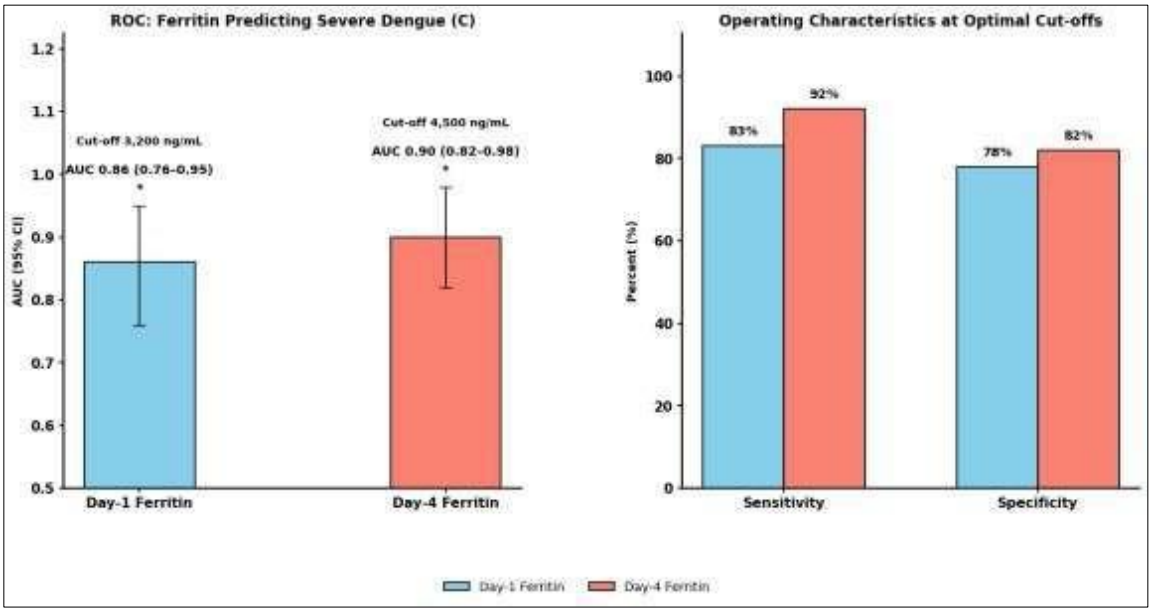
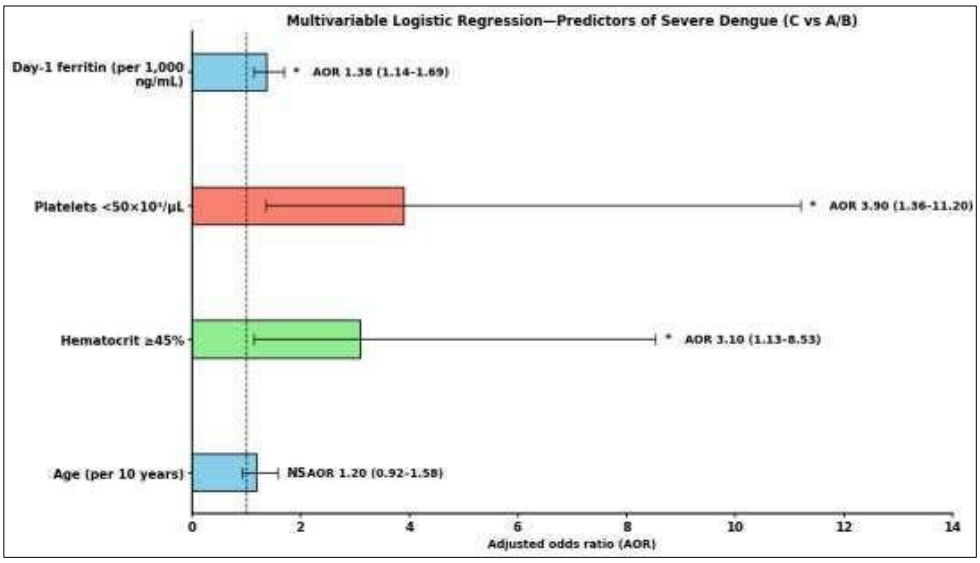


Table 8: Multivariable Logistic Regression—Predictors of Severe Dengue (C vs A/B)

Predictor	Adjusted OR (95% CI)	p-value
Day-1 ferritin (per 1,000 ng/mL)	1.38 (1.14–1.69)	0.001
Platelets <50×10³/µL	3.90 (1.36–11.2)	0.012
Hematocrit ≥45%	3.10 (1.13–8.53)	0.028
Age (per 10 years)	1.20 (0.92–1.58)	0.180
Model performance	AUC = 0.90	0.001

Multivariable logistic regression identified day-1 ferritin with an adjusted OR of 1.38 (95% CI: 1.14–1.69, p = 0.001), platelet count <50×10³/µL with OR 3.90 (95% CI: 1.36–11.2, p = 0.012), and hematocrit ≥45% with OR 3.10 (95% CI: 1.13–8.53, p = 0.028) as predictors of severe dengue, while age per 10 years was not significant (OR 1.20, 95% CI: 0.92–1.58, p= 0.180); the model showed strong performance with AUC = 0.90 (p =0.001).

Figure 8: Multivariable Logistic Regression—Predictors of Severe Dengue (C vs A/B)



Discussion

The study population comprised 60 adult patients with confirmed dengue infection, with severity distribution of 20 patients in Category A, 28 in Category B, and 12 in Category C. Socioeconomic, educational, occupational, and lifestyle characteristics were evaluated to explore possible demographic determinants of disease severity. Dengue fever continues to pose a substantial clinical and public health challenge due to its unpredictable progression and the potential for rapid deterioration into severe forms characterized by plasma leakage, hemorrhage, and organ dysfunction. The investigation aimed to evaluate the relationship between serum ferritin levels and clinical severity of dengue fever in adults. In addition, the study sought to compare ferritin levels across WHO 2009 severity categories (A, B, and C), determine the predictive value of Day-1 and Day-4 ferritin measurements for severe dengue, establish optimal diagnostic cut-off values using ROC analysis, and examine the association of ferritin with platelet count, hematocrit, and hepatic enzyme levels (AST and ALT) in order to understand its potential role as a biomarker of disease progression.

Conclusion

the study confirms that serum ferritin serves as a valuable biomarker in adult dengue infection, providing meaningful insight into disease progression, inflammatory activity, and risk of complications. Measurement of ferritin at admission and during early hospitalization offers an accessible and clinically practical method for identifying patients at risk of severe outcomes. Incorporating ferritin estimation alongside routine hematological and biochemical parameters may therefore enhance early triage, guide monitoring strategies, and support timely clinical intervention in patients with dengue infection.

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