

Research Article

Association of Serum Ferritin and Lactate Dehydrogenase with Severity of Dengue in Hospitalised Children: A Prospective Observational Study

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ABSTRACT

Background: Early recognition of severe dengue in children remains clinically important, particularly in endemic settings where deterioration may occur during the critical phase. Serum ferritin and lactate dehydrogenase (LDH) are accessible laboratory markers potentially associated with hyper-inflammation and tissue injury.

Objectives: To assess the association of serum ferritin and LDH with severe dengue in hospitalised children, and to compare their performance at the predefined laboratory thresholds.

Methods: This prospective observational study included 100 children aged 1-12 years with laboratory confirmed dengue admitted to the Department of Paediatrics, PSP Medical College Hospital and Research Institute, Kancheepuram District, Tamil Nadu, during 2025. Serum ferritin and LDH were measured on admission between day 3 and day 7 of illness. Severe dengue status was compared with biomarker categories and selected clinical findings.

Results: Twenty children (20.0%) developed severe dengue. Ferritin was 300 ng/mL or higher in 18/20 severe cases and 1/80 non-severe cases, while LDH was 250 U/L or higher in 19/20 severe cases and 5/80 non-severe cases. Concurrent elevation of both markers occurred in 18/20 severe cases and in none of the non-severe cases. Elevated ferritin, elevated LDH and combined elevation were each significantly associated with severe dengue (all $p < 0.001$). Ferritin elevation had sensitivity 90.0% and specificity 98.8%; LDH elevation had sensitivity 95.0% and specificity 93.8%; combined elevation retained sensitivity of 90.0% with specificity of 100.0%.

Conclusion: Serum ferritin and LDH were strongly associated with severe dengue in this paediatric hospital cohort. Their combined elevation may aid early risk stratification, although validation in larger multicentre cohorts is needed before adopting fixed thresholds for prediction.

Keywords: Children, Dengue, Ferritin, Lactate Dehydrogenase, Severe Dengue, Biomarkers.

INTRODUCTION

The burden of dengue has expanded substantially in recent decades, and children in endemic regions continue to present with a spectrum ranging from uncomplicated febrile illness to plasma leakage, shock, bleeding and organ dysfunction.[1] The World Health Organization classifies symptomatic infection as dengue with or without warning signs and severe dengue, a distinction intended to guide triage, monitoring and fluid management.[2] In India, the National Centre for Vector Borne Diseases Control similarly emphasises early recognition of warning signs and severe

disease, because timely supportive treatment remains central to reducing mortality.[3]

The clinical challenge is that progression is not always apparent during the first assessment. The febrile phase may be deceptively stable, while vascular permeability, haemoconcentration and circulatory compromise emerge around defervescence. Viral factors and host immune responses, including endothelial activation and dysregulated inflammatory signalling, contribute to severe disease.[4] In a busy paediatric unit, this makes a practical severity marker valuable only when it is affordable,

quickly available, and interpretable alongside bedside findings.

Ferritin has attracted attention because it is not merely an index of iron storage during acute illness. As an acute-phase reactant, marked hyperferritinaemia may reflect intense immune activation and coagulation disturbances in dengue.[5] A systematic review and meta-analysis found higher ferritin concentrations among patients with severe dengue than among non-severe cases, while also noting considerable heterogeneity in measurement timing and cut-off selection.[6] Paediatric observations have similarly described rising ferritin concentrations in dengue haemorrhagic fever compared with uncomplicated dengue, suggesting that the marker may be clinically informative during the evolving phase of illness.[7]

Lactate dehydrogenase (LDH) is a widely available marker of cellular injury and may increase with hepatic involvement, tissue hypoperfusion or severe systemic inflammation. In dengue, higher LDH values have been described among children.[8] Ferritin and LDH assess related but not identical biological processes. Their concurrent measurement may therefore strengthen clinical risk stratification rather than relying on either marker in isolation. This study evaluated the association of serum ferritin and LDH with severe dengue among hospitalised children in a tertiary paediatric centre in Kancheepuram District, Tamil Nadu.

MATERIALS AND METHODS

Study Design and Setting

A prospective observational study was undertaken in the Department of Paediatrics, PSP Medical College Hospital and Research Institute, Tamil Nadu, India, in the year 2025 over a period of 3 months.

Study Population

Children admitted with laboratory-confirmed dengue fever were considered for inclusion. Dengue confirmation was defined by NS1 antigen positivity during day 1 to day 4 of fever or dengue IgM ELISA positivity after day 4 of illness.

Inclusion Criteria

Children aged 1-12 years who were admitted with dengue confirmed by NS1 antigen or dengue IgM ELISA were included.

Exclusion Criteria

Children younger than 1 year and children with chronic liver disease or chronic inflammatory disease were excluded.

Sample Size

The sample size was calculated using the formula $n = Z^2pq/d^2$, with $Z=1.96$ at 95% confidence, an expected severe dengue proportion of 4.2%, $q=95.8\%$ and absolute precision of 5%. The resulting minimum sample size was 62; after accounting for a 10% non-response allowance, the minimum requirement was 68. A total of 100 children were enrolled.

Clinical Assessment and Outcome Classification

Relevant history and examination findings were recorded in a predesigned proforma. Warning signs assessed included vomiting and abdominal pain. Platelet count, haematocrit and ultrasonographic findings were documented. Children were followed clinically for the development of severe dengue and complications, including dengue shock syndrome, dengue haemorrhagic fever, dengue encephalopathy and multiorgan dysfunction syndrome.

Biomarker Measurement and Analytical Categories

Serum ferritin and serum LDH were measured on the day of admission, when the child was between day 3 and day 7 of illness. The reported ferritin categories were <300, 300-1000 and >1000 ng/mL; for binary marker analysis, ferritin values in the latter two categories were treated as elevated (≥ 300 ng/mL). The reported LDH categories were <250, 250-1000 and >1000 U/L; LDH values ≥ 250 U/L were treated as elevated. Concurrent marker elevation denoted elevation of both ferritin and LDH.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of PSP Medical College Hospital and Research Institute. Written informed consent was obtained from the parent or guardian, and participant confidentiality was maintained.

Statistical Analysis

Data were entered in Microsoft Excel and analysed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarised as frequencies and percentages. Associations between severity and categorical clinical variables were evaluated using the chi-square test where appropriate; Fisher's exact test was used for threshold-based biomarker comparisons and binary ultrasound comparisons because of sparse cell counts. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and

accuracy with Wilson 95% confidence intervals (CI) were calculated using severe dengue as the outcome. A p-value <0.05 was considered statistically significant.

RESULTS

One hundred children with confirmed dengue were included. Severe dengue occurred in 20 children (20.0%), while 80 (80.0%) had non-

severe dengue. Children aged 7 to <10 years were the largest age group, and males accounted for 54.0% of participants. Sixty-nine children had one or more warning signs at presentation. Baseline clinical and laboratory distributions are shown in Table 1, while the severity distribution is illustrated in Figure 1.

Table 1. Clinical and Laboratory Profile of Children with Dengue Fever (N=100).

Variable	Frequency	Percentage (%)
Age Group		
<3 Years	9	9.0
3 To <7 Years	27	27.0
7 To <10 Years	33	33.0
10-12 Years	31	31.0
Sex		
Male	54	54.0
Female	46	46.0
Duration Of Fever At Presentation		
<4 Days	35	35.0
>4 Days	65	65.0
Warning Signs		
None	31	31.0
Vomiting Only	34	34.0
Abdominal Pain Only	15	15.0
Vomiting And Abdominal Pain	20	20.0
Platelet Count At Presentation		
<50,000/Cu.Mm	24	24.0
50,000-100,000/Cu.Mm	39	39.0
>100,000/Cu.Mm	37	37.0
Haematocrit		
<35%	27	27.0
35-40%	47	47.0
>40%	26	26.0
Ultrasonography		
No Abnormal Finding	48	48.0
Any Abnormal Finding	52	52.0

Values are expressed as number and percentage. cu.mm: cubic millimetre.

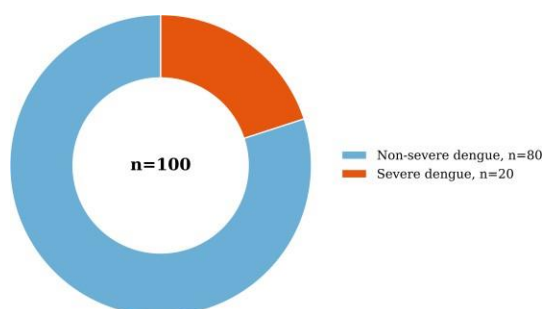


Figure 1. Severity Distribution among Children with Dengue Fever. Donut chart shows the proportion of children classified as non-severe and severe dengue.

Children with severe dengue more often had both vomiting and abdominal pain, lower platelet categories, and abnormal ultrasound findings. Of the 20 severe cases, seven had ascites alone and six had ascites with pleural

effusion. Warning-sign pattern and platelet category were significantly associated with severe dengue, while haematocrit category was not (Table 2).

Table 2. Clinical and Investigation Findings According To Dengue Severity.

Variable	Non-Severe Dengue (N=80)	Severe Dengue (N=20)	P-Value
Warning Signs			
None	28 (35.0)	3 (15.0)	0.015
Vomiting Only	28 (35.0)	6 (30.0)	
Abdominal Pain Only	13 (16.3)	2 (10.0)	
Vomiting And Abdominal Pain	11 (13.8)	9 (45.0)	
Platelet Count			
<50,000/Cu.Mm	16 (20.0)	8 (40.0)	0.015
50,000-100,000/Cu.Mm	29 (36.3)	10 (50.0)	
>100,000/Cu.Mm	35 (43.8)	2 (10.0)	
Haematocrit			
<35%	24 (30.0)	3 (15.0)	0.198
35-40%	38 (47.5)	9 (45.0)	
>40%	18 (22.5)	8 (40.0)	
Ultrasonography			
No Abnormal Finding	48 (60.0)	0 (0.0)	<0.001
Any Abnormal Finding	32 (40.0)	20 (100.0)	

Values are n (% within severity group). Chi-square test was used for warning signs, platelet count and haematocrit; Fisher's exact test was used for the binary ultrasonography comparison.

Ferritin values were 300 ng/mL or higher in 18 of 20 children with severe dengue, compared

with 1 of 80 children with non-severe dengue. Similarly, LDH values were 250 U/L or higher in 19 severe cases and five non-severe cases. Concomitant elevation of both biomarkers was seen in 18 severe cases and in no non-severe child (Table 3). Their distributions by severity are presented in Figures 2 and 3.

Table 3. Distribution of Serum Ferritin and LDH According To Dengue Severity.

Biomarker Category	Non-Severe Dengue (N=80)	Severe Dengue (N=20)	Total
Serum Ferritin			
<300 Ng/MI	79 (98.8)	2 (10.0)	81
300-1000 Ng/MI	1 (1.3)	5 (25.0)	6
>1000 Ng/MI	0 (0.0)	13 (65.0)	13
Serum LDH			
<250 U/L	75 (93.8)	1 (5.0)	76
250-1000 U/L	5 (6.3)	2 (10.0)	7
>1000 U/L	0 (0.0)	17 (85.0)	17
Concurrent Marker Elevation			
Ferritin And LDH Elevated	0 (0.0)	18 (90.0)	18
Not Both Elevated	80 (100.0)	2 (10.0)	82

Values are n (% within severity group). Binary threshold comparisons for ferritin ≥ 300 ng/mL, LDH ≥ 250 U/L and concurrent

elevation were each statistically significant by Fisher's exact test (all $p < 0.001$). LDH: lactate dehydrogenase.

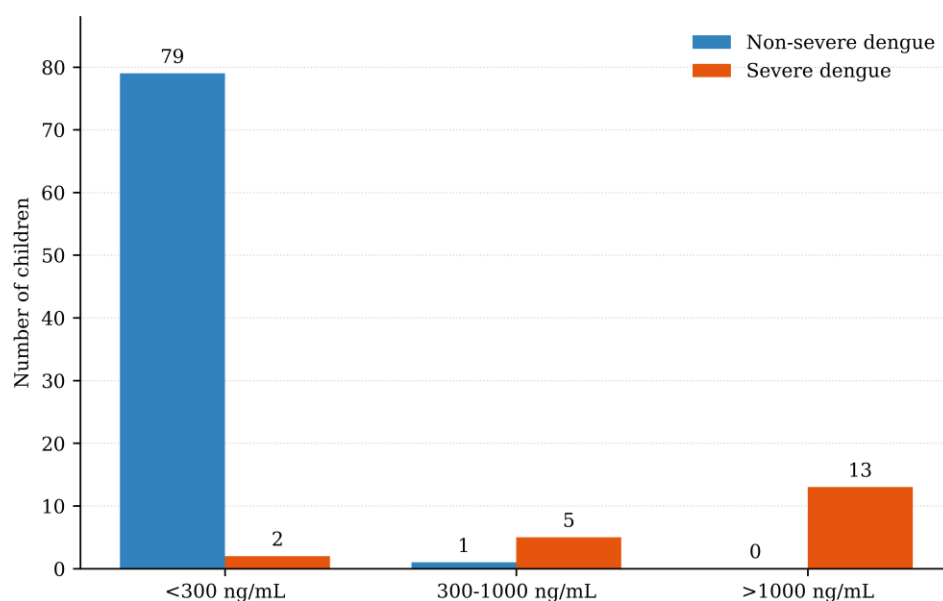


Figure 2. Serum Ferritin Categories According To Dengue Severity.

Grouped bars display numbers of children in each ferritin category.

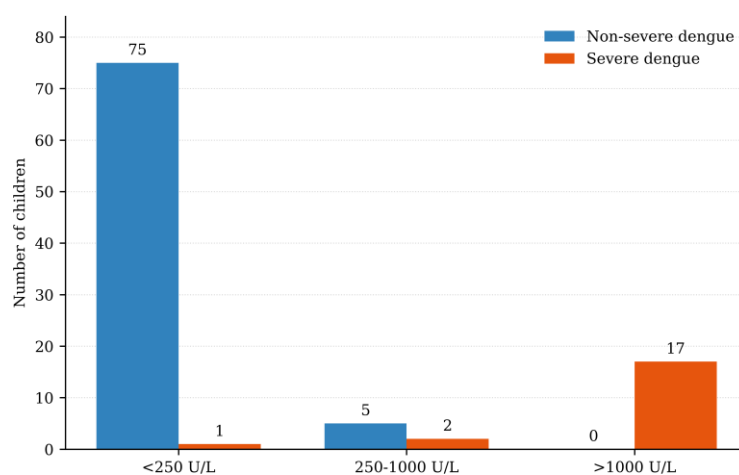


Figure 3. Serum LDH Categories According To Dengue Severity.

Grouped bars display numbers of children in each LDH category.

At the predefined analytical threshold, ferritin elevation showed a sensitivity of 90.0% and specificity of 98.8% for severe dengue. LDH elevation was slightly more sensitive (95.0%) but less specific (93.8%). Concurrent elevation

of ferritin and LDH was present in 90.0% of severe cases and in no non-severe child, corresponding to a specificity of 100.0% and an accuracy of 98.0% in this cohort (Table 4 and Figure 4).

Table 4. Diagnostic Performance of Serum Ferritin and LDH Thresholds for Severe Dengue.

Marker Threshold	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy % (95% CI)
Ferritin ≥300 Ng/MI	90.0 (69.9-97.2)	98.8 (93.3-99.8)	94.7 (75.4-99.1)	97.5 (91.4-99.3)	97.0 (91.5-99.0)
LDH ≥250 U/L	95.0 (76.4-99.1)	93.8 (86.2-97.3)	79.2 (59.5-90.8)	98.7 (92.9-99.8)	94.0 (87.5-97.2)
Ferritin And LDH	90.0 (69.9-	100.0 (95.4-	100.0 (82.4-	97.6 (91.5-	98.0 (93.0-

Elevated	97.2)	100.0)	100.0)	99.3)	99.4)
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Confidence intervals are Wilson 95% confidence intervals. PPV: positive predictive value; NPV: negative predictive value; CI:

confidence interval; LDH: lactate dehydrogenase.

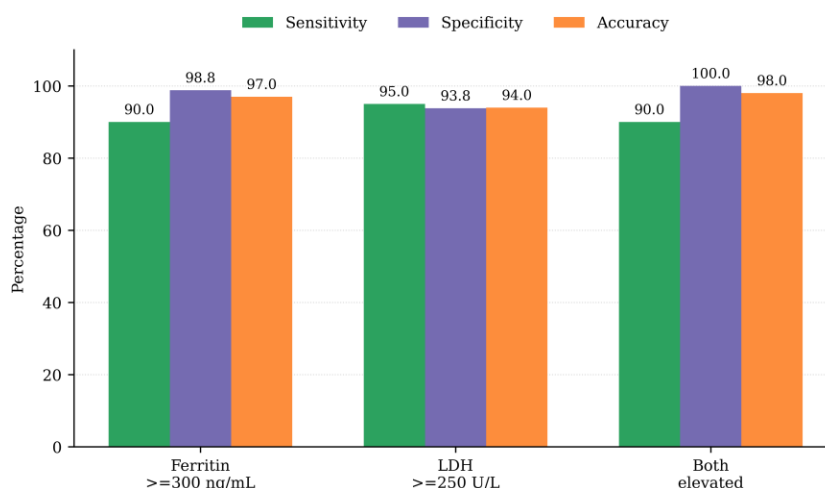


Figure 4. Comparative Performance of Ferritin and LDH Thresholds for Severe Dengue. Grouped bars show point estimates for sensitivity, specificity and accuracy.

Among the 20 children with severe dengue, the documented complications were dengue shock syndrome alone in 13 cases, dengue haemorrhagic fever alone in one case, dengue encephalopathy alone in one case, dengue shock syndrome with dengue haemorrhagic fever in two cases, dengue shock syndrome with dengue encephalopathy in one case and multi-organ dysfunction syndrome in two cases.

DISCUSSION

The central observation of this study is clinically direct: severe dengue was uncommon compared to non-severe disease, yet it clustered strongly with elevated serum ferritin and LDH. Eighteen of the 20 severe cases had raised values of both markers, while no child in the non-severe group had concurrent elevation. This finding is important in a paediatric referral unit because a readily available pair of laboratory tests may help direct closer observation during the phase when shock or organ dysfunction can evolve rapidly.

The ferritin pattern is consistent with earlier evidence linking hyperferritinaemia to severe dengue. Soundravally et al. described substantially higher ferritin in severe dengue and proposed its prognostic utility in an Indian cohort.[9] Petchiappan et al. similarly reported that elevated ferritin measured early in illness was associated with severe dengue among

patients in Tamil Nadu.[10] In adult dengue, Suresh et al. found ferritin to be a useful predictor of severe disease both at admission and later during hospitalisation.[11] More recently, an Indian prospective study by Goyal et al. again supported ferritin as a severity marker, while the systematic review by Shukla et al. highlighted that universal cut-offs remain uncertain because study methods and timing vary.[6,12] The present paediatric findings therefore support association and triage relevance, but do not establish a universal diagnostic threshold.

Elevated LDH also showed a strong relationship with severe dengue. Nineteen of 20 severe cases had LDH at or above 250 U/L, and all children with LDH greater than 1000 U/L belonged to the severe group. Sirikutt and Kalayanarooj described higher LDH levels among severe dengue phenotypes and examined its value for severity prediction.[8] In a paediatric intensive care cohort, Equebal and Dhanawade reported that higher LDH was associated with severe manifestations and complications.[13] LDH is not specific for dengue severity; it may reflect hepatic injury, tissue hypo-perfusion or systemic cellular stress. Its practical value lies in being routinely obtainable and interpretable alongside clinical trajectory and other markers.

The relationship between ultrasound abnormalities and severe dengue was equally notable. Every severe case had an abnormal

ultrasonographic finding, most commonly ascites alone or ascites with pleural effusion. In children with dengue, early evidence of plasma leakage on imaging has been reported as a useful marker of progression to severe disease.[14] Gallbladder wall oedema and other sonographic patterns have also been associated with greater clinical severity.[15] In Indian paediatric wards, where bedside ultrasound access is increasingly available, imaging can complement laboratory markers when warning signs are emerging but haemodynamic deterioration is not yet obvious.

There are practical implications. A child with abdominal pain and vomiting, falling platelet category, ultrasonographic evidence of leakage and concurrent ferritin-LDH elevation may warrant intensified observation even before overt shock occurs. Yet biomarkers should not displace serial examination, urine output monitoring, haematocrit trends, or careful fluid management. National guidance remains centred on clinical classification and supportive treatment, and laboratory markers can only strengthen, not replace, that approach.[3]

This study has limitations. It was conducted at a single tertiary care institution and included 100 children, of whom only 20 had severe dengue. Biomarkers were assessed once between day 3 and day 7 of illness rather than at a fixed fever-day or serially, limiting evaluation of temporal change. The study did not include children with other febrile illnesses, so diagnostic discrimination for dengue itself cannot be inferred. Threshold analyses were based on categorical biomarker groups; receiver operating characteristic analysis, multivariable modelling and external validation were not available. Finally, as severe dengue may already have been clinically evident at the time of sampling in some children, the results should be interpreted as an association useful for risk stratification rather than proof of independent early prediction.

CONCLUSION

Serum ferritin and LDH were strongly associated with severe dengue among hospitalised children in this tertiary paediatric cohort. LDH elevation was marginally more sensitive, while ferritin elevation was more specific; concurrent elevation of both markers showed the highest specificity and accuracy. These tests may support closer monitoring of children at risk of severe disease, but larger

multicentre studies with serial measurements and validated cut-offs are needed before their routine use as standalone predictive markers.

Declarations

Ethics Approval: Approved by the Institutional Ethics Committee of PSP Medical College Hospital and Research Institute.

Informed Consent: Written informed consent was obtained from parents or guardians.

Source of Funding: Nil.

Conflict of Interest: None declared.

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