Section: Paediatrics

Original Research Article

SERUM FERRITIN AS AN EARLY PREDICTOR OF DISEASE SEVERITY IN PEDIATRIC DENGUE: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Dengue fever remains a major cause of pediatric morbidity, and early identification of children at risk for severe disease is essential. Serum ferritin, an acute-phase reactant, has emerged as a potential biomarker for predicting disease severity. This study aimed to evaluate the diagnostic utility of serum ferritin levels in NS1-positive pediatric dengue cases.

Materials and Methods: A prospective observational study was conducted among 120 children ≤14 years diagnosed with dengue by NS1 antigen positivity at a tertiary care center. Clinical examination, laboratory evaluation including platelet count, CRP, liver function tests, and serial serum ferritin levels (days 3, 4, and 5), were recorded. Participants were categorized into dengue without warning signs (DWOWS), dengue with warning signs (DWWS), and severe dengue as per WHO criteria. Statistical analysis included descriptive statistics, comparison of laboratory parameters, and correlation assessment.

Results: Severe dengue cases exhibited significantly lower platelet counts and higher CRP, transaminases, and serum ferritin levels compared with non-severe cases ($p < 0.001$). Ferritin levels increased progressively from day 3 to day 5 across all groups, with markedly higher values in severe dengue (876–1573 ng/mL). A moderate to strong negative correlation was found between ferritin and platelet count ($r = –0.62$). Day-wise ferritin cut-offs demonstrated high sensitivity and diagnostic accuracy for predicting severe dengue. Clinical outcomes were favourable, with 98.3% recovering and no mortality.

Conclusion: Serum ferritin is a reliable, early indicator of disease severity in pediatric dengue and can serve as an effective adjunct biomarker for clinical triage, especially during the critical phase of illness.

Keywords: Pediatric dengue, Disease severity, Serum ferritin, Thrombocytopenia, NS1 antigen.

INTRODUCTION

Dengue fever stands as a significant arboviral infection globally, with an estimated 390 million cases occurring each year, of which approximately 96 million present clinically.[1] The impact is most severe in tropical and subtropical areas, where frequent outbreaks disproportionately harm children, who are particularly susceptible to the swift advancement of severe dengue, plasma leakage, and shock.[2] Identifying children who are at risk for severe disease at an early stage is crucial for effective triage, determining monitoring intensity, and allocating resources in busy pediatric units.[3]

The existing classifications from the WHO focus on clinical warning signs to assess severity; however, these indicators may manifest later in the progression of the illness and can be influenced by subjective interpretation. In this context, straightforward laboratory indicators that represent the fundamental inflammatory and immune response are being examined more frequently. Serum ferritin, an acute-phase reactant synthesized by activated macrophages and hepatocytes, has been identified as a noteworthy candidate.[4,5] A recent systematic review and meta-analysis conducted by Shukla et al. revealed that serum ferritin levels are markedly elevated in cases of severe dengue compared to non-severe instances, showcasing substantial effect sizes across various

studies and classifications, thereby reinforcing its potential as a prognostic biomarker.[6]

Research in pediatrics provides additional evidence for the practical application of ferritin in clinical settings. Kiran and Yerra found that children suffering from severe dengue exhibited significantly elevated ferritin levels between days 3 and 5 of their illness compared to those with non-severe cases, leading to the conclusion that ferritin serves as an effective predictor of early progression.[7] Meghana and Pradeep noted elevated ferritin levels during the critical phase, especially in children experiencing dengue shock syndrome, and identified a significant correlation with severe thrombocytopenia and the need for intensive care.[8] In a recent study, Jha et al. demonstrated that extreme hyperferritinemia (>10,000 ng/mL) in pediatric patients with severe dengue infection admitted to the PICU correlated with increased mortality and complications.[9] The findings indicate that repeated serum ferritin measurements in children with dengue could serve as a practical and objective method for predicting disease severity, enhancing both clinical evaluations and standard laboratory tests. Hence this study was designed to evaluate the diagnostic utility of serum ferritin levels in NS1-positive pediatric dengue cases.

MATERIALS AND METHODS

A prospective observational study was conducted in the Department of Pediatrics, Government Medical College, Mulugu, Telangana, from June 2024 to September 2025. The study aimed to evaluate the clinical profile, biochemical parameters, and disease progression in children diagnosed with dengue fever, with a particular focus on haematological and inflammatory markers such as platelet count and serum ferritin. A total of 120 consecutively presenting children who fulfilled the diagnostic criteria for dengue infection were enrolled after confirming NS1 antigen positivity. All eligible participants were recruited from the outpatient and inpatient services of the department.

Inclusion Criteria:

Children confirmed dengue infection based on a positive NS1 antigen test, age ≤14 years, belonging to the pediatric age group of both genders, presence of clinical signs and symptoms suggestive of dengue fever, willingness to participate, documented through informed consent obtained from a parent or legal guardian.

Exclusion Criteria:

Children with chronic liver disease, chronic kidney disease, congenital heart disease, autoimmune disorders, absence of a positive NS1 antigen report, systemic inflammatory diseases, and not willing to participate were excluded.

Approval for the study was obtained from the Institutional Ethics Committee of Government Medical College, Mulugu prior to initiation. Written informed consent was obtained from the parents or legal guardians of all participants.

All the children were undergone a complete clinical assessment. The demographic profile, presenting symptoms, duration of illness, signs of dehydration, hemodynamic status, and presence of warning signs were recorded in a pre-designed case record form. A detailed medical history was obtained, including previous hospitalizations, medication history, nutritional status, and immunization status. A 2-3ml of peripheral venous blood was collected by a trained phlebotomist using aseptic precautions. Samples were transferred to sterile plain vacutainers for biochemical assays and EDTA tubes for haematological parameters. The laboratory investigations such as complete blood profile, C-reactive protein, liver function tests including AST, ALT, serum bilirubin, albumin, renal function tests including urea and creatinine, serum ferritin levels, measured using Chemiluminescence Immunoassay.

All enrolled children were closely monitored for disease progression, development of dengue warning signs, and clinical outcomes. Daily monitoring on vital signs, hydration status, and serial platelet counts was recorded. Children were categorized according to WHO dengue classification into dengue without warning signs, dengue with warning signs, and severe dengue.

Statistical Analysis: Data analysis was performed using SPSS v.26.0. Descriptive statistics were used to summarize demographic and baseline clinical characteristics. Categorical variables were analysed using the chi-square test or Fisher's exact test when appropriate. Continuous variables were expressed as mean and standard deviation and compared using Student's t-test based on the data distribution. A p-value <0.05 was considered statistically significant.

RESULTS

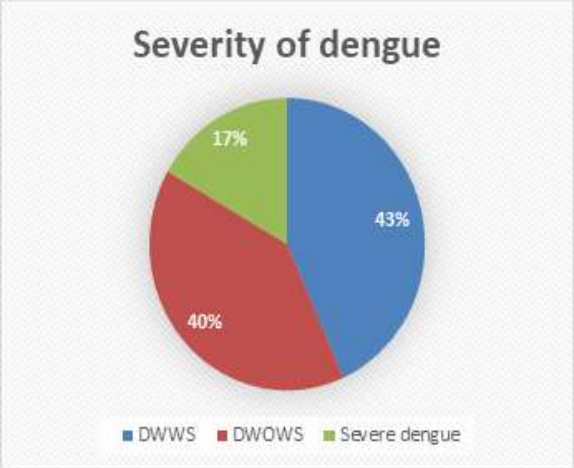

Figure 1: Severity Classification of Dengue (WHO 2009).

*DWWS- Dengue with warning signs, DWOWS- Dengue without warning signs.

Table 1: Demographic and clinical profile of Study Participants (n = 120)

Demographic/clinical profile	Total no of cases (n=120)	
	Frequency	Percentage
Age (In years)		
1-5	32	26.7
6-10	46	38.3
11-14	42	35.0
Gender		
Male	68	56.7
Female	52	43.3
Clinical profile		
Fever	120	100
Body pains	82	68.3
Vomiting	56	46.7
Abdominal pain	44	36.7
Rash	28	23.3
Bleeding manifestations	18	15.0
Hepatomegaly	26	21.7

Table 2: Comparison of laboratory parameters by dengue severity category.

Laboratory markers	DWWS (n=52)	DWOWS (n=48)	Severe Dengue (n=20)	p-value
	Mean ± SD	Mean ± SD	Mean ± SD	
Platelet count (cells/mm³)	112,654 ± 18,532	84,327 ± 19,410	55,829 ± 14,220	0.001
CRP (mg/L)	19.68±4.30	16.94±3.56	14.76±2.89	0.001
Albumin (gm./dl)	3.51±1.37	3.45±1.58	3.39±1.95	0.001
Serum ferritin (ng/mL)	480 ± 120	690 ± 150	1,120 ± 260	0.001
AST (U/L)	62 ± 22	94 ± 30	146 ± 40	0.001
ALT (U/L)	48 ± 15	78 ± 24	110 ± 32	0.001
CRP (mg/L)	12 ± 4	19 ± 5	29 ± 7	0.001

Table 3: Comparison of serum ferritin levels and dengue severity category.

Serum ferritin levels	DWWS (n=52)	DWOWS (n=48)	Severe Dengue (n=20)
	Mean ± SD	Mean ± SD	Mean ± SD
Day 3	822.68 ± 82.81	478.39 ± 56.18	724.8 ± 22.78
Day 4	985.99 ± 112.25	620.82 ± 71.39	799.3 ± 44.72
Day 5	1367.45 ± 128.16	704.16 ± 78.60	818.6 ± 30.56

The correlation coefficient (r = –0.62) indicates a moderate to strong negative correlation, suggesting that higher serum ferritin levels are associated with lower platelet counts. This inverse relationship reflects the underlying inflammatory response and disease severity in dengue infection, where elevated ferritin a known acute-phase reactant—correlates with increased immune activation and potential progression toward severe disease manifestations.

Table 4: Outcome of Study Participants

Outcome	Frequency	Percentage
Improved and discharged	118	98.3
Required PICU care	14	11.7
Mortality	0	0

DISCUSSION

Pediatric morbidity from dengue fever remains high in endemic areas, and early detection of children at risk of severe illness is a clinical priority. A prospective observational study of 120 NS1-positive children aged ≤14 years revealed that serum ferritin levels substantially increased in severe dengue infections from day 3 to day 5 of illness compared to non-severe cases. Ferritin had a moderate to strong negative connection with platelet count (r = –0.62), and day-wise ferritin cut-offs predicted severe illness with good sensitivity and specificity. These data suggest serum ferritin is a useful, early biomarker for pediatric dengue risk categorization.

Our findings support the emerging literature linking Hyperferritinemia to dengue severity. Shukla et al.'s comprehensive review and meta-analysis of different cohorts found that severe dengue patients had higher blood ferritin levels, with substantial effect sizes and excellent discriminative performance for severe outcomes.[6] Our findings that children with warning signals and severe dengue had more ferritin than those without warning signs are supported by our meta-analysis.

Many clinical investigations have examined ferritin as a prognostic marker in children and adults. In an Indian prospective observational research, Goyal et al. found that severe dengue adults had considerably higher mean serum ferritin levels and that ferritin was marginally negatively connected with platelet count and positively correlated with hospital stay.[10] In our pediatric sample, greater ferritin levels were related with more severe thrombocytopenia and clinical

severity, confirming the ferritin–platelet inverse association across age groups and contexts.

Kiran and Yerra examined serum ferritin as an indicator of disease severity in 74 pediatric dengue patients and found that severe dengue patients had significantly higher ferritin levels on days 3, 4, and 5, with mean values similar to our study.[7] They found that serial ferritin estimation may accurately predict early disease development. Another pediatric research by Meghana and Pradeep found that ferritin levels peaked in the critical phase, were greater in children with dengue shock syndrome or acute respiratory distress, and linked with severe thrombocytopenia and prolonged hospital stays.[8] Our results and these pediatric investigations support ferritin inclusion in hospitalized dengue laboratory panels.

Ferritin levels on days 3-5 were sensitive and accurate for severe dengue in our population. According to dengue pathophysiology, the febrile to critical phase change occurs around days 3 to 7. Lakshmanan et al.'s retrospective PICU study of severe dengue children found extremely high median ferritin levels (above 8,000 ng/mL) and highly correlated with WHO severe dengue classifications.[11] Data show that indicated Hyperferritinemia is common in critically sick children who need intensive care, supporting our results in a hospitalized pediatric population with both severe and non-severe cases.

Ferritin's position as an acute-phase reactant and indication of macrophage activation and cytokine-driven inflammation supports its use as a dengue severity biomarker. Pro-inflammatory cytokines like IL-6 and TNF-α cause ferritin synthesis, which increases with immunological activation and liver involvement. Shukla et al. note that ferritin is part of a “Hyperferritinemia response” in severe viral and inflammatory diseases, including dengue, which is linked to capillary leak and organ failure.[12] We found that ferritin rises with clinical severity and biochemical abnormalities (transaminase, CRP, thrombocytopenia) supports this mechanism.

Ferritin levels may rise dramatically in severe dengue and dengue-associated hemophagocytic lymphohistiocytosis (HLH), which is a clinical issue. See noted in a recent narrative review that dengue-associated HLH is underdiagnosed yet deadly and that high ferritin levels typically indicate its existence.[6] Our ferritin values were lower than those reported in HLH, but the constant rise in severe dengue supports the idea that ferritin ranges from mild increases predicting severe dengue to extremely high levels indicating secondary HLH. Children with extremely high ferritin, recurrent fever, cytopenias, or organ failure need thorough clinical examination.

CONCLUSION

Overall, the findings from the present study contribute to growing evidence supporting serum ferritin as a valuable biomarker for predicting dengue severity in pediatric populations. Its correlation with thrombocytopenia, liver dysfunction, and clinical severity underscores its pathophysiological relevance. Early measurement of ferritin during the initial days of illness could aid clinicians in triaging children who are likely to deteriorate, thereby improving outcomes.

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