



# Biochemical and Hematological Markers as Predictors of Severity in Pediatric Dengue: A Case Series Analysis

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## Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case report

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## ABSTRACT

Dengue fever is a mosquito-borne viral illness caused by the dengue virus with a spectrum of presentations ranging from mild febrile illness to severe life-threatening conditions such as Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). Early identification of severe

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cases is crucial to reduce morbidity and mortality especially in vulnerable pediatric populations. This case series presents four pediatric patients with varying degrees of dengue severity emphasizing the role of biochemical and hematological parameters in assessing disease severity and guiding clinical management. Parameters such as ferritin, LDH, lactate, liver enzymes (AST, ALT), platelet count and coagulation markers (PT, APTT) and PCV were observed to correlate with disease severity and recovery. The normalization of these markers with treatment highlighted their utility in monitoring patient progress. These findings reinforce the importance of incorporating a broad biochemical assessment in dengue management protocols to optimize patient outcomes.

*Keywords: Dengue fever; biochemical markers; pediatric dengue; disease severity.*

## 1. INTRODUCTION

Dengue fever caused by the dengue virus (a Flavivirus) remains a major global health concern particularly in tropical and subtropical regions. According to the World Health Organization (WHO) approximately 390 million dengue infections occur annually with a significant proportion resulting in severe complications such as Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) (World Health Organization, 2019). These severe forms are characterized by plasma leakage, severe thrombocytopenia, coagulopathy, elevated Packed Cell Volume and multi-organ dysfunction leading to high mortality rates if not managed promptly (Guzman & Harris, 2015).

The clinical manifestations of dengue are often non-specific in the early stages making it challenging to distinguish between mild and severe cases (Gubler, 1998). As the disease progresses systemic inflammation, immune activation and cellular damage contribute to the pathophysiology resulting in elevated levels of biochemical markers such as ferritin, lactate dehydrogenase (LDH), liver enzymes (AST and ALT), elevated PCV and prolonged coagulation times (PT and APTT) and a sharp decline in platelet count further indicate severe disease. These markers are invaluable in predicting the progression to severe dengue guiding clinical decisions and prioritizing care (Kularatnam et al., 2019; Azin et al., 2012).

Several studies have highlighted the utility of biochemical and hematological markers in identifying severe dengue cases. Elevated ferritin levels, often used as an indicator of immune activation and inflammation have been shown to correlate with severe disease progression and poor outcomes (Goya et al., 2024). Likewise, elevated LDH and liver enzymes reflect cellular injury and tissue damage due to viral infection

and immune responses (Reeves et al., 2023). Furthermore, coagulation abnormalities such as prolonged PT and APTT are common in severe dengue and contribute to the pathogenesis of DHF and DSS (Adane & Getawa, 2021).

Dengue progresses through three clinical phases: the febrile, critical and recovery phases. The febrile phase typically lasts 2–7 days presenting with high fever, headache, myalgia and rash, accompanied by nonspecific laboratory findings such as leukopenia and mild thrombocytopenia (Guzman & Harris, 2015). The critical phase follows as fever subsides marking a period of increased vascular permeability, plasma leakage and potential shock or hemorrhage. During this phase severe thrombocytopenia, elevated hematocrit, prolonged coagulation times and high levels of inflammatory markers like ferritin and LDH may be observed indicating heightened disease severity (Simmons et al., 2012). The recovery phase is characterized by reabsorption of leaked plasma, improving platelet counts and normalization of biochemical parameters such as AST, ALT and lactate levels signifying recovery (Trung et al., 2010). Close monitoring across these phases is essential to identify complications early and guide effective management (Martina et al., 2009).

This case series focuses on four pediatric patients with dengue fever ranging from DSS to DHF who presented with significant abnormalities in key biochemical and hematological parameters. These cases underline the importance of monitoring markers such as ferritin, LDH, AST/ALT, lactate and coagulation tests (PT/APTT) along with platelet count to stratify risk and manage severe dengue effectively. By analyzing these cases we aim to provide a framework for utilizing these parameters in clinical practice to improve outcomes in dengue patients.

This study is particularly relevant in pediatric populations who are more vulnerable to the complications of dengue (Bhatt et al., 2013). The findings emphasize the need for early recognition of severe cases through comprehensive laboratory assessments and timely therapeutic interventions (World Health Organization, 2017).

## 2. CASE PRESENTATIONS

Case 1 involved a 6-year-old female patient who presented with Dengue Shock Syndrome. Her laboratory findings revealed extreme elevations in inflammatory and biochemical markers, including ferritin, LDH, AST (SGOT), ALT (SGPT), and normal PCV. Additionally, she exhibited coagulopathy with prolonged PT and APTT, along with thrombocytopenia. Her hemoglobin level remained normal. Following 10 days of intensive treatment, all her parameters returned to normal, highlighting the effectiveness of prompt and aggressive management.

Case 2 involved a 12-year-old female patient who presented to the emergency department with high fever and was diagnosed with dengue fever through a positive NS1 antigen test. She demonstrated severe biochemical derangements, including elevated ferritin, LDH,

AST, and ALT levels. Her platelet count was critically low, and her hemoglobin was mildly reduced. Coagulation parameters were also affected, with prolonged PT and APTT. After 12 days of treatment, the patient showed significant improvement with normalization of platelet count, hemoglobin levels, and a reduction in ferritin, LDH, and liver enzymes.

Case 3 was a 1-year-old male infant admitted with Dengue Hemorrhagic Fever. He presented with severe thrombocytopenia and anemia. His inflammatory markers were markedly elevated and the patient also had high lactate levels reflecting tissue hypoxia and prolonged PT and APTT, indicating coagulopathy. Liver enzymes were elevated. After appropriate treatment, all these parameters normalized, demonstrating recovery from severe dengue.

Case 4 involved an 8-month-old male infant admitted with Dengue Hemorrhagic Fever. The patient exhibited critical abnormalities, including severe thrombocytopenia, elevated ferritin, LDH, and lactate levels. Liver enzymes were markedly elevated, and coagulation parameters were severely prolonged. Despite these severe findings, the patient responded well to treatment with normalization of ferritin, LDH, liver enzymes, platelet count, PCV and coagulation parameters.

**Table 1. Shows the level of hematology and biochemistry parameters for case 1**

Days	Platelet (200-490 10 <sup>3</sup> /μl)	PCV (34-40 %)	Hb (11.0-14.0 gm/dL)	APTT (22.3-32.4 seconds)	LDH (85- 222 U/L)	Ferritin (13-150 ng/ml)	SGOT (10-35 U/L)	SGPT (0- 33 U/L)
Day 1	58000	34.2	12.0	86.6	6561	54126	3290	1043
Day 3	65000	28.4	10.1	68.6	6288	34701	2712	807
Day 5	42000	37.6	11.0	40.4	3257	11971	833	510
Day 7	56000	32.3	10.6	36.8	2588	10711	534	380
Day 9	115000	30.1	10.3	32.4	2037	7600	368	315
Day 11	89000	29.7	10.2	31.8	1314	3476	189	166
Day 15	215000	28.5	9.9	29.4	795	1143	81	106

**Table 2. Displays the level of hematology and biochemistry parameters for case 2**

Days	Platelet (170-450 10 <sup>3</sup> /μl)	PCV (38- 46 %)	Hb (12-16 gm/dL)	APTT (22.3-32.4 seconds)	LDH (85-222 U/L)	Ferritin (13-150 ng/ml)	SGOT (10-35 U/L)	SGPT (0- 33 U/L)
Day 1	46000	33.2	10.4	83.3	2862	55494	1338	260
Day 3	37000	30.9	9.7	56.4	2723	39360	907	251
Day 4	55000	28.1	9.3	38.6	2582	21805	915	261
Day 6	102000	28.5	9.4	34.4	1985	14425	483	199
Day 8	201000	27.3	8.9	30.4	1544	9039	289	160
Day 11	607000	29.7	9.7	31.6	551	1539	85	75

**Table 3. Indicates the level of hematology and biochemistry parameters for case 3**

Day	Platelet (200-550 10 <sup>3</sup> /µl)	PCV (30-38 %)	Hb (11.1-14.1 gm/dL)	APTT (22.3-32.4 seconds)	LDH (85-222 U/L)	Ferritin (30-400 ng/ml)	SGOT (10-50 U/L)	SGPT (0-41 U/L)	Lactate (0.5-2.2 mmol/l)
Day 1	36000	27.0	10.8	70.5	3557	36628	1466	374	6.10
Day 2	58000	22.4	7.5	54.9	4378	45776	3905	1029	2.13
Day 4	96000	26.3	8.8	44.8	2228	15669	1380	856	1.46
Day 6	153000	25.7	8.4	34.1	985	4308	239	250	1.19
Day 8	168000	25.5	8.2	30.5	356	2500	99	101	1.84
Day 9	207000	28.6	9.1	23.5	198	856	88	76	1.66

**Table 4. Exhibited the level of hematology and biochemistry parameters for case 4**

Day	Platelet (200-550 10 <sup>3</sup> /µl)	PCV (30-38 %)	Hb (11.1-14.1 gm/dL)	APTT (28-32 seconds)	Lactate (0.5-2.2 mmol/l)	LDH (85-222 U/L)	Ferritin (13-150 ng/ml)	SGOT (10-35 U/L)	SGPT (0-33 U/L)
Day 1	24000	34.7	12	123.6	6.59	3263	28687	2473	659
Day 2	21000	22.3	8.5	142.0	2.53	2971	21299	2085	480
Day 4	69000	23.3	7.4	76.8	3.03	993	16653	1516	408
Day 6	83000	22.7	7.0	39.8	1.38	587	3879	443	231
Day 8	93000	20.8	6.5	28.4	1.88	223	863	200	117
Day 9	118000	23.6	7.8	22.9	1.69	201	168	94	92

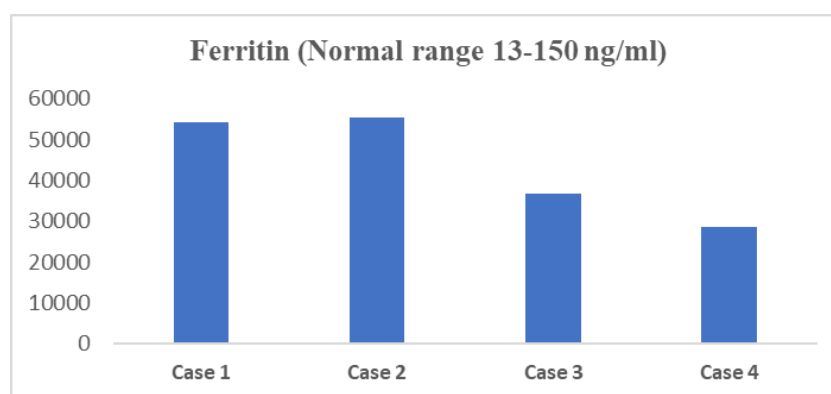
### 3. DISCUSSION

Dengue fever caused by the dengue virus is a systemic viral infection transmitted by Aedes mosquitoes. It has a broad clinical spectrum ranging from self-limiting febrile illness to severe manifestations such as Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). The pathophysiology of severe dengue involves immune response dysregulation, plasma leakage, coagulopathy and multi-organ damage leading to significant morbidity and mortality. This case series highlights the importance of key biochemical and hematological parameters in assessing disease severity, monitoring progression and guiding therapeutic decisions.

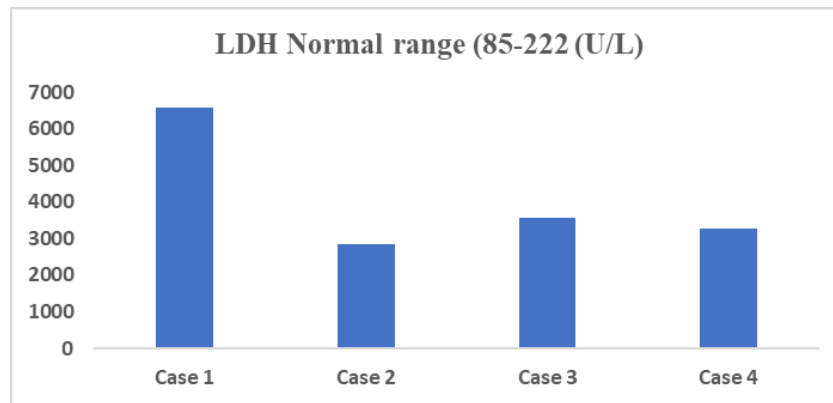
#### 3.1 Mechanisms Behind Biochemical and Hematological Changes

##### 3.1.1 Ferritin as a Marker of Inflammation

Ferritin an acute-phase reactant is significantly elevated in severe dengue due to systemic inflammation triggered by viral infection. Inflammatory mediators stimulate ferritin synthesis which acts as a marker of the body's response to infection. Extremely elevated ferritin levels as observed in our cases (ranging from 8,365 to 54,126 ng/mL) correlate with severe disease. High ferritin levels may also reflect oxidative stress and immune overactivation which can exacerbate disease progression (Kalayanarooj, 2011). Ferritin 366-fold increases compared with normal shown in Fig. 1.



**Fig. 1. shows the elevated level of ferritin in all 4 cases**



**Fig. 2. shows the flouted variation of LDH in all 4 cases**

### 3.1.2 LDH as an Indicator of Cellular Damage

Lactate dehydrogenase (LDH) is a key marker of cellular injury. In severe dengue plasma leakage and hypovolemia result in tissue hypoperfusion leading to cellular stress and anaerobic metabolism. Elevated LDH levels in our cases (1,553 to 6,561 U/L) signify widespread cell damage particularly in the liver and hematopoietic systems and are reflective of the metabolic disturbances caused by hypoperfusion (Kasarabada et al., 2023). LDH shows 29-fold increases compared with normal range as shown in Fig. 2.

### 3.1.3 Lactate in Severe Dengue

Elevated lactate levels as seen in cases 3 and 4 indicate tissue hypoxia due to reduced oxygen delivery caused by plasma leakage and hypovolemia. Inadequate tissue perfusion forces cells into anaerobic metabolism resulting in the accumulation of lactate. The high lactate levels (6.1 and 6.59 mmol/L) observed in these patients highlight the critical need for aggressive fluid resuscitation to restore perfusion and oxygenation (Sirikutt & Kalayanarooj, 2014).

### 3.1.4 Hemoglobin and PCV

In dengue, hemoglobin and PCV levels are initially elevated due to plasma leakage caused by increased vascular permeability. However, as the disease progresses, fluid replacement therapy can lead to hemodilution, reducing both hemoglobin and PCV. Additionally, dengue-induced hemorrhage, bone marrow suppression, and immune-mediated hemolysis further contribute to their reduction. These mechanisms collectively reflect the dynamic changes in

hemoglobin and PCV during the illness (Simmons et al., 2012).

### 3.1.5 Liver Enzymes (AST/ALT) and Hepatic Involvement

Hepatic dysfunction is a prominent feature of severe dengue often attributed to direct viral invasion of hepatocytes and immune-mediated liver injury. Elevated AST (SGOT) and ALT (SGPT) levels in all cases particularly the disproportionately high AST levels in cases 1 (3,290 U/L) and 4 (2,473 U/L) underscore significant liver involvement. Liver injury impairs protein synthesis, detoxification and coagulation processes contributing to disease severity (Swamy et al., 2021).

### 3.1.6 Thrombocytopenia and Coagulation Abnormalities

Thrombocytopenia is a hallmark of severe dengue and results from increased platelet consumption, bone marrow suppression and immune-mediated destruction. Prolonged PT and APTT as seen in all cases indicate coagulopathy which contributes to hemorrhagic complications and worsening shock. The normalization of platelet counts and coagulation parameters with treatment demonstrates the reversibility of these changes when appropriate care is provided (Ho et al., 2013).

The cases presented in this study align with the classical progression of dengue through its febrile, critical and recovery phases. In the febrile phase patients exhibited high fever and elevated inflammatory markers such as ferritin and LDH consistent with early immune activation (Sami et al., 2023). The critical phase characterized by plasma leakage, coagulopathy and severe

thrombocytopenia was evident in all cases particularly in Cases 3 and 4 where prolonged APTT, high lactate levels and marked liver enzyme elevation reflected severe systemic involvement (Kalayanarooj, 2011). Recovery phase markers including normalization of platelet counts, ferritin and liver enzymes highlight the reversibility of biochemical derangements with timely intervention. These findings emphasize the importance of recognizing the transition between phases to tailor management and improve outcomes in severe pediatric.

#### 4. CONCLUSION

The findings from this case series reinforce the importance of comprehensive biochemical and hematological assessments in managing dengue patients particularly in pediatric populations. Monitoring parameters such as ferritin, LDH, AST/ALT, lactate, and coagulation tests provides valuable insights into disease severity guiding timely and effective interventions. Early identification of high-risk patients through these markers enables clinicians to prioritize resources and optimize therapeutic strategies such as aggressive fluid resuscitation, close hemodynamic monitoring and targeted supportive care. Additionally regular monitoring of these markers during treatment provides a dynamic picture of patient recovery and therapeutic efficacy.

This case study highlights the need to integrate these parameters into routine diagnostic and monitoring protocols for dengue management particularly in resource-limited settings where early recognition of severity can significantly reduce morbidity and mortality. Future research aimed at establishing standardized thresholds and predictive algorithms for these markers will further enhance the ability of clinicians to combat severe dengue effectively. By fostering a deeper understanding of the biochemical and hematological markers of disease severity this study contributes to improving patient outcomes and advancing clinical management in dengue-endemic regions.

#### CONSENT

It is not applicable.

#### ETHICAL APPROVAL

It is not applicable.

#### DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declares that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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