Section: Pediatrics

Original Research Article

PROGNOSTIC SIGNIFICANCE OF HEPATIC DYSFUNCTION IN CHILDREN WITH FEVER AND THROMBOCYTOPENIA: A PROSPECTIVE OBSERVATIONAL STUDY

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Received *: 10/09/2026*
Received in revised form *: 08/10/2026*
Accepted *: 21/10/2026*

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DOI: 10.70034/ijmedph.2026.4.232

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (4); 1523-1527

ABSTRACT

Background: Fever with thrombocytopenia is a common cause of pediatric hospital admission and may be associated with significant hepatic involvement. Liver dysfunction may reflect disease severity and contribute to adverse clinical outcomes. This study aimed to evaluate the correlation between hepatic dysfunction and clinical outcomes in children admitted with fever and thrombocytopenia.

Materials and Methods: This prospective observational study included 124 children aged 1 month to 12 years admitted with fever and thrombocytopenia. Clinical characteristics, hematological parameters, liver function tests, and coagulation profiles were recorded. Hepatic dysfunction was assessed using abnormalities in transaminases, bilirubin, serum albumin, and coagulation parameters. Participants were followed until discharge or death, and associations between hepatic dysfunction and clinical outcomes were analysed.

Results: Hepatic dysfunction was observed in 58 (46.8%) children, while 32 (25.8%) developed adverse clinical outcomes. Children with hepatic dysfunction had a significantly higher frequency of adverse outcomes than those without hepatic dysfunction (46.6% vs. 7.6%; $p<0.001$). Elevated AST and ALT levels, hyperbilirubinemia, hypoalbuminemia, and elevated INR were significantly associated with poor outcomes. Hepatic dysfunction remained independently associated with adverse clinical outcomes (adjusted OR: 6.84; 95% CI: 2.31–20.27; $p<0.001$).

Conclusion: Hepatic dysfunction was significantly associated with adverse clinical outcomes in children with fever and thrombocytopenia. Early assessment of liver function may improve risk stratification and facilitate timely monitoring and management.

Keywords: Hepatic dysfunction, Fever, Thrombocytopenia, Children, Liver function tests, Clinical outcome.

INTRODUCTION

Fever with thrombocytopenia is a frequently encountered clinical syndrome among hospitalized children, particularly in tropical and subtropical countries where vector-borne and other infectious diseases are endemic. The underlying causes are diverse and include dengue, scrub typhus, malaria, septicaemia, enteric fever, viral infections, and other undifferentiated febrile illnesses. The overlapping clinical manifestations of these conditions often make early diagnosis challenging, while the development of thrombocytopenia may indicate increased disease severity or systemic involvement. Studies of pediatric febrile thrombocytopenia have demonstrated considerable etiological variation, with dengue and other infectious diseases accounting for a substantial proportion of cases.[1,2]

Although platelet count is routinely monitored in children with acute febrile illnesses, thrombocytopenia alone may not adequately reflect the extent of organ involvement or predict clinical outcome. Acute systemic infections can affect

multiple organs, including the liver, through direct microbial injury, inflammatory responses, endothelial dysfunction, hypoperfusion, and immune-mediated mechanisms. Liver involvement may manifest as hepatomegaly, elevated aminotransferases, hyperbilirubinemia, hypoalbuminemia, or coagulation abnormalities. Consequently, abnormalities in liver function tests may provide additional information regarding the severity and progression of acute febrile illness.

Scrub typhus represents an important example of a febrile illness in which thrombocytopenia and hepatic involvement frequently coexist. In a prospective study of hospitalized children with acute febrile illness in North India, thrombocytopenia was consistently observed in children with scrub typhus, and most affected children also demonstrated elevated serum transaminases.[3] Similarly, Ganesh et al. found that elevated AST and thrombocytopenia at admission were associated with an increased risk of complications among children with scrub typhus.[4] Other pediatric studies have also documented hepatomegaly, elevated liver enzymes, shock, acute kidney injury, and other complications in severe scrub typhus, emphasizing the relationship between hepatic involvement and systemic disease severity.[5] The prognostic importance of hepatic involvement is also supported by studies examining acute liver injury in hospitalized children. The clinical spectrum ranges from isolated biochemical abnormalities to significant hepatic dysfunction associated with systemic illness and unfavourable outcomes.[6] Furthermore, recent pediatric dengue research has demonstrated that abnormalities in liver function parameters may be associated with disease severity, intensive care admission, and mortality.[7]

Despite the clinical importance of hepatic involvement in individual infectious diseases, limited studies have evaluated hepatic dysfunction as a prognostic factor among children presenting broadly with fever and thrombocytopenia. Evaluating liver function parameters alongside platelet count may therefore provide a more comprehensive assessment of disease severity and facilitate early identification of children at risk of adverse outcomes. Hence, the present study was undertaken to evaluate the correlation between hepatic dysfunction and clinical outcome in children admitted with fever and thrombocytopenia.

MATERIALS AND METHODS

This hospital-based prospective observational study was conducted in the Department of Paediatrics at Pratima Relief Institute of Medical Sciences, Hanamkonda, Telangana and MNR Medical College and Hospital, Sangareddy from April 2025 to June 2026. A total of 124 children aged 1 month to 12 years admitted with fever and thrombocytopenia, defined as a platelet count of <150,000/µL, and availability of baseline laboratory investigations required for assessment of hepatic function were included using consecutive sampling after obtaining written informed consent from their parents or legal guardians. The study protocol was approved by the institutional ethics committee and confidentiality of data was maintained. Children with known chronic liver disease, hematological malignancies, inherited thrombocytopenic disorders, immune thrombocytopenia, or drug-induced thrombocytopenia were excluded.

Detailed demographic and clinical information, including age, sex, duration of fever, bleeding manifestations, jaundice, hepatomegaly, splenomegaly, and other clinical features, was recorded using a predesigned case proforma. Laboratory investigations included complete blood count, platelet count, liver function tests comprising serum bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total protein, and serum albumin, along with coagulation parameters including prothrombin time, activated partial thromboplastin time, and international normalized ratio. Relevant etiological investigations were performed according to clinical suspicion and institutional protocols.

Hepatic dysfunction was assessed based on abnormalities in liver biochemical and synthetic function parameters. All enrolled children were followed throughout their hospital stay until discharge or death. Clinical outcomes, including duration of hospital stay, bleeding complications, shock, intensive care requirement, organ dysfunction, and mortality, were documented. The association between hepatic dysfunction and clinical outcomes was evaluated.

Statistical analysis: Data were extracted to Microsoft Excel sheet and analysed using SPSS v.26.0. Continuous variables were expressed as mean and standard deviation, while categorical variables were presented as frequency and percentage. The Chi-square test was used for categorical variables, and the independent t-test was applied for continuous variables as appropriate. Correlation analysis was performed using Pearson's correlation coefficient. A $p<0.05$ was considered statistically significant.

RESULTS

Table 1: Demographic and clinical characteristics of study participants (n=124).

Demographic / clinical Characteristic	Total cases (n=124)	
	Frequency	Percentage
Age group		
<1 year	12	9.7%
1–5 years	47	37.9%
6–12 years	65	52.4%
Gender		
Male	69	55.6%
Female	55	44.4%
Residence		
Urban	73	58.9%
Rural	51	41.1%
Etiological diagnosis		
Dengue fever	48	38.7%
Fever with thrombocytopenia – undifferentiated	31	25%
Scrub typhus	16	12.9%
Malaria	11	8.9%
Enteric fever	7	5.6%
Sepsis	6	4.8%
Other febrile illnesses	5	4%
Clinical characteristics		
Vomiting	58	46.8%
Abdominal pain	42	33.9%
Hepatomegaly	39	31.5%
Bleeding manifestations	28	22.6%
Splenomegaly	26	21%
Jaundice	17	13.7%
Altered sensorium	9	7.3%
Ascites	8	6.5%
Shock at admission	14	11.3%
Platelet count (/µL)		
<10,000	9	7.3%
10,000-30,000	26	21%
30,001-50,000	24	19.4%
50,001-100,000	39	31.5%
100,001-150,000	26	21%

Table 2: Baseline laboratory parameters and levels.

Parameter	Mean ± SD
Haemoglobin (g/dL)	10.2±1.8
Total leukocyte count (/mm³)	7,840±3,260
Platelet count (/µL), (median)	58,000 (32,000-96,000)
Haematocrit (%)	35.8±5.4
AST (U/L), (median)	72 (38-156)
ALT (U/L), (median)	61 (32-132)
Total bilirubin (mg/dL)	1.3±1.1
Serum albumin (g/dL)	3.5±0.6
INR	1.19±0.28

Table 3: Distribution of hepatic function abnormalities and severity of hepatic dysfunction.

Parameter	Normal	Abnormal
	Frequency (%)	Frequency (%)
Hepatic function abnormalities		
AST	68 (54.8%)	56 (45.2%)
ALT	71 (57.3%)	53 (42.7%)
Total bilirubin	104 (83.9%)	20 (16.1%)
Serum albumin	96 (77.4%)	28 (22.6%)
PT/INR	101 (81.5%)	23 (18.5%)
Overall hepatic dysfunction	66 (53.2%)	58 (46.8%)
Severity of hepatic dysfunction		
No hepatic dysfunction	66	53.2%
Mild hepatic dysfunction	29	23.4%
Moderate hepatic dysfunction	19	15.3%
Severe hepatic dysfunction	10	8.1%

Table 4: Association between hepatic dysfunction and clinical outcome.

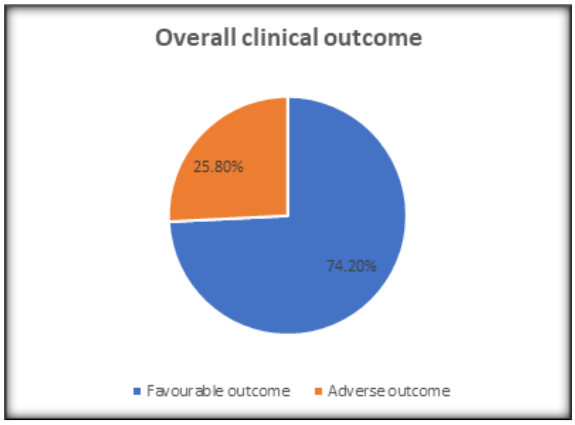
Variable	Favourable outcome (n = 92)	Adverse outcome (n = 32)	p-value
Hepatic dysfunction			
Hepatic dysfunction	31 (53.4%)	27 (46.6%)	0.001
No hepatic dysfunction	61 (92.4%)	5 (7.6%)	-
Hepatic dysfunction vs outcome			
No dysfunction	61 (49.2%)	5	0.001
Mild dysfunction	20 (16.1%)	9	
Moderate dysfunction	8 (6.45%)	11	
Severe dysfunction	3	7	

Table 5: Comparison of hepatic parameters between outcome groups

Parameter	Favourable outcome (n=92)	Adverse outcome (n=32)	p-value
AST (U/L), median	48 (31-89)	214 (132-356)	0.001
ALT (U/L), median	41 (27-78)	176 (104-288)	0.001
Total bilirubin (mg/dL)	0.9±0.5	2.5±1.4	0.001
Serum albumin (g/dL)	3.7±0.5	2.9±0.6	0.001
INR	1.08±0.16	1.51±0.39	0.001

Table 6: Association between AST Levels, ALT levels and outcome.

AST & ALT level (U/L)	Favourable	Adverse	p-value
AST levels vs outcome			
Normal	55 (44.4%)	3(2.4%)	0.001
1-3×ULN	24 (19.4%)	8 (6.5%)	
3-5×ULN	9 (7.2%)	11 (8.8%)	
>5×ULN	4 (3.2%)	10 (8.06%)	
ALT levels vs outcome			
Normal	59 (47.58%)	5 (4.03%)	0.001
1-3×ULN	20 (16.12%)	8 (6.5%)	
3-5×ULN	9 (7.2%)	10 (8.06%)	
>5×ULN	4 (3.2%)	9 (7.2%)	



Graph 1: Overall clinical outcome.

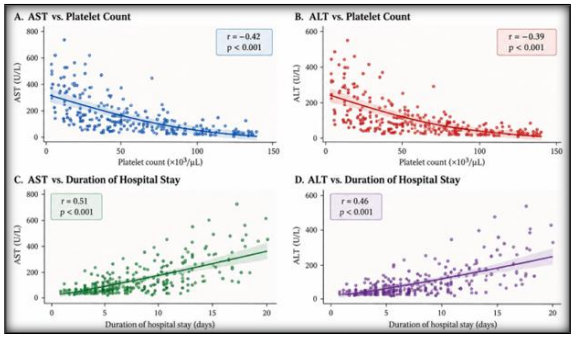


Figure 1: Correlation analysis in children with fever and thrombocytopenia.

DISCUSSION

Dengue fever was the most common etiology in the present study, which is consistent with the epidemiological importance of dengue as a major cause of acute febrile illness and thrombocytopenia in tropical regions. Hepatic involvement is well recognized in pediatric dengue and ranges from asymptomatic elevation of liver enzymes to severe hepatitis and acute liver failure. Mohan et al. reported abnormal hepatic enzymes in a substantial proportion of children with dengue, with greater derangement among those with dengue haemorrhagic fever and dengue shock syndrome.[8] Similarly, Jagadishkumar et al. observed elevated AST and ALT levels in 93% and 78% of children, respectively, and demonstrated more pronounced hepatic dysfunction among children with severe dengue.[9] The comparatively lower proportion of hepatic dysfunction in the present study may be attributed to the inclusion of children with different etiologies of fever and thrombocytopenia rather than dengue alone.

Elevated AST and ALT were among the most frequent biochemical abnormalities observed in the present study. Children with adverse outcomes had significantly higher transaminase levels, and increasing AST and ALT values were associated with lower platelet counts and prolonged hospitalization. This finding is supported by Prasad and Bhriguvanshi, who demonstrated that transaminase elevation was more frequent in severe dengue and that severe hepatitis was associated with shock, acute kidney injury, altered sensorium, acute liver failure,

and mortality.[10] A larger pediatric study by Srivastava et al. similarly reported that the severity of liver injury and aminotransferase elevation increased significantly with dengue severity.[11] These observations suggest that marked elevation of hepatic enzymes should not be considered an isolated laboratory abnormality but may reflect systemic disease severity and evolving multiorgan involvement.

The inverse correlation between platelet count and hepatic enzyme levels observed in the present study is clinically important. Severe thrombocytopenia was significantly associated with adverse outcomes and frequently coexisted with greater hepatic dysfunction. Both abnormalities may result from the intensity of systemic inflammation, endothelial dysfunction, viral or infectious tissue injury, and altered coagulation. Similar observations have been reported in pediatric dengue, where thrombocytopenia, elevated ALT, hypoalbuminemia, and other clinical manifestations were associated with poorer outcomes.[12] Furthermore, hepatic involvement should not be interpreted exclusively in the context of dengue. In pediatric scrub typhus, elevated hepatic transaminases have also been associated with thrombocytopenia, hypoalbuminemia, severe disease, and prolonged hospitalization.[13]

Synthetic liver dysfunction also appeared to have prognostic relevance in the present study. Children with adverse outcomes demonstrated higher bilirubin and INR values and lower serum albumin concentrations. These findings indicate that assessment of hepatic involvement should extend beyond transaminases alone. Bilirubin elevation, coagulopathy, and hypoalbuminemia may represent more substantial hepatic impairment or systemic disease progression. Previous studies have similarly identified elevated bilirubin and INR as markers associated with poor outcomes, particularly in severe dengue and acute liver failure.[10,14] In pediatric dengue-associated acute liver failure, low albumin and multisystem involvement have also been identified among factors associated with mortality.[14] Multivariable analysis in the present study demonstrated hepatic dysfunction as an independent predictor of adverse clinical outcome. This finding supports the potential value of early liver function assessment in children admitted with fever and thrombocytopenia. Routine measurement of AST, ALT, bilirubin, albumin, and coagulation parameters may help identify children requiring closer monitoring and timely escalation of care. However, hepatic dysfunction should be interpreted together with platelet count, hemodynamic status, renal function, and the underlying etiology.

CONCLUSION

Hepatic dysfunction appears to be an important indicator of disease severity and adverse clinical outcome in children admitted with fever and thrombocytopenia. Abnormalities in liver function parameters, particularly elevated AST and ALT levels, hyperbilirubinemia, hypoalbuminemia, and coagulopathy, were associated with poorer clinical outcomes and prolonged hospitalization. The association between hepatic dysfunction and severe thrombocytopenia further suggests that combined assessment of hematological and hepatic parameters may improve early risk stratification. Routine evaluation of liver function tests may therefore help identify children requiring closer monitoring and timely intensive care. Early recognition and appropriate management of hepatic involvement could potentially improve clinical outcomes in this vulnerable population.

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