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Original Research Article

DYSFUNCTION AS A PREDICTOR OF SEVERITY IN PEDIATRIC DENGUE: A COMPARATIVE STUDY OF CHILDREN WITH AND WITHOUT WARNING SIGNS

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ABSTRACT

Background: Dengue fever is a major public health challenge in tropical regions, and hepatic involvement is increasingly recognized as an important predictor of disease severity, particularly in children. Early identification of biochemical abnormalities is essential for risk stratification and prevention of complications. This study aims to compare clinical features, liver function abnormalities, and coagulation parameters between children with dengue fever without warning signs.

Materials and Methods: This prospective observational study was conducted at Government Medical College, Mulugu, from April 2024 to September 2025. A total of 100 children aged 1–18 years with serologically confirmed dengue IgM positivity were enrolled and stratified into Group 1 (dengue without warning signs; n=48) and Group 2 (dengue with warning signs; n=52). Clinical features, haematological parameters, liver function tests, and coagulation profiles were recorded and compared using appropriate statistical methods.

Result: Children with warning signs demonstrated significantly higher frequencies of petechiae, icterus, splenomegaly, vomiting, abdominal pain, and melena. Mean levels of AST (117.6 vs. 626.04 U/L), ALT (76.4 vs. 392.1 U/L), total bilirubin (0.79 vs. 2.45 mg/dL), and ALP (181.5 vs. 361.3 U/L) were markedly elevated in Group 2 compared with Group 1 ($p<0.01$). Hypoalbuminemia and prolonged PT/aPTT were also significantly more common in Group 2.

Conclusion: Hepatic dysfunction is significantly more pronounced in pediatric dengue patients with warning signs. Elevated AST, bilirubin, ALP, and coagulation abnormalities serve as valuable indicators of disease severity. Routine liver function and coagulation monitoring should be included in the evaluation of children with suspected severe dengue.

Keywords: Dengue fever, Pediatric dengue, Hepatic involvement, Warning signs, Coagulation abnormalities.

INTRODUCTION

Dengue fever (DF) is an emerging viral infection transmitted by Aedes mosquitoes, caused by one of four serotypes of the dengue virus (DENV 1–4). This represents a significant public health issue in tropical and subtropical areas, with an estimated 390 million infections each year, of which around 96 million exhibits clinically.[1] Children represent a significant percentage of symptomatic infections and exhibit a higher likelihood of developing severe disease, including dengue with warning signs (DWS) and severe dengue, attributable to immunological and physiological vulnerabilities.

Liver involvement is a recognized manifestation of dengue and significantly contributes to morbidity in pediatric populations. Hepatic dysfunction in dengue varies from mild, transient increases in aminotransferases to severe hepatitis and acute liver failure.[3] The elevation of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) is commonly noted, with AST levels generally

surpassing ALT. This pattern indicates potential injury from both hepatic and extra-hepatic sources, including muscle damage.[4,5] The mechanisms of hepatic involvement encompass direct viral cytopathic effects, immune-mediated injury, cytokine storm, microvascular dysfunction, and ischemic hepatopathy due to plasma leakage.[3]

Numerous studies indicate that the extent of liver enzyme elevation is associated with disease severity, highlighting the significance of biochemical markers for early risk stratification.[6] Hypoalbuminemia, hyperbilirubinemia, and abnormal coagulation parameters are more frequently observed in patients exhibiting warning signs or severe dengue, indicating impaired hepatic synthetic function.[7] In pediatric patients, hepatomegaly, persistent vomiting, abdominal pain, and bleeding tendencies frequently coexist with biochemical abnormalities and may precede the advancement to severe dengue.[2,6]

Considering the increasing prevalence of dengue in India and worldwide, it is crucial to comprehend liver involvement in pediatric dengue for prompt diagnosis, monitoring, and complication prevention. This study compares clinical features, liver function abnormalities, and coagulation parameters in children with dengue fever, distinguishing between those without warning signs and those with warning signs, to emphasize the role of hepatic dysfunction as a marker of disease severity.

MATERIALS AND METHODS

This prospective observational study was carried out at Government Medical College, Mulugu, from April 2024 to September 2025. A total of 100 consecutive children exhibiting signs and symptoms of dengue fever, confirmed positive for dengue IgM in the blood and demonstrating liver involvement, were recruited from the outpatient department of pediatrics.

Inclusion criteria consisted of serologically confirmed (IgM positive) dengue fever patients aged 1-18 years, regardless of gender, who consented to participate. Exclusion criteria included IgM negative dengue-like illnesses, children under 1 year and over 18 years of age, children with pre-existing liver diseases, and participants unwilling to participate.

Informed consent was obtained from study participants or their parents/guardians. The institutional ethics committee approved the study protocol. The study participants were categorized into two groups based on the presence of warning signs associated with dengue fever. Group 1 includes cases of dengue fever without warning signs, while Group 2 encompasses cases with warning signs.

All study participants underwent assessments for complete blood counts and serum levels of dengue NS1, IgM, and IgG antibodies. Liver function tests, including serum total bilirubin, total protein, serum albumin, serum globulin, aspartate transaminase, alanine transaminase, alkaline phosphatase, prothrombin index, activated partial thromboplastin time, bleeding time, and clotting time, were assessed. The data were analysed using SPSS version 26.0. Demographic variables were expressed in terms of frequency and percentages through descriptive statistics. The associations between categorical variables were analysed using the Chi-square test. Continuous variables were expressed as the mean with the standard deviation. A p-value less than 0.05 was deemed statistically significant.

RESULTS

Table 1: Sociodemographic characteristics of study participants (n=100)

Demographic data	Group 1 (n=48) Frequency (%)	Group 2 (n=52) Frequency (%)
Age (In years)		
1-4	14(29.2%)	17(32.7%)
5-9	24(50.0%)	25(48.1%)
10-15	10(20.8%)	10(19.2%)
Gender		
Male	27(56.2%)	23(44.2%)
Female	21(43.8%)	29(55.8%)

Table 2: Comparison of signs and symptoms in children with and without warning signs of dengue fever

Signs & symptoms	Group 1 (n=48) Frequency (%)	Group 2 (n=52) Frequency (%)	p-value
Signs			
Edema	12 (25%)	20 (38.5%)	0.15
Lymphadenopathy	43 (89.6%)	44 (84.6%)	0.46
Petechiae	24 (50%)	38 (73.1%)	0.01
Icterus	02 (4.2%)	22 (42.3%)	0.00
Hepatomegaly	46 (95.8%)	51 (98.1%)	0.51
Splenomegaly	18 (37.5%)	31 (59.6%)	0.02
Symptoms			
Fever	48 (100%)	52 (100%)	-
Headache	22 (45.8%)	36 (69.2%)	0.01
Vomiting	26 (54.2%)	42 (80.8%)	0.01
Pain abdomen	28 (58.3%)	45 (86.5%)	0.01
Arthralgia	06 (12.5%)	13 (25%)	0.11

Malena	02 (4.2%)	12 (23.1%)	0.01
Rash	28 (58.3%)	38 (73.1%)	0.12

Table 3: Comparison of liver function tests and coagulation parameters among children with and without warning signs of dengue fever

Laboratory parameters	Group 1 (n=48) Frequency (%)	Group 2 (n=52) Frequency (%)	t-value	p-value
Liver function tests				
Total bilirubin	0.79±067	2.45±2.15	-5.14	0.00
Direct bilirubin	0.28±0.59	1.47±1.64	-4.79	0.00
Indirect bilirubin	0.51±0.13	1.00±0.74	-4.49	0.00
Sr. proteins	6.30±0.83	5.82±1.02	2.58	0.01
Albumin	3.17±0.52	2.70±0.51	4.59	0.00
AST	117.6±124.6	626.04±1253.5	-2.80	0.01
ALT	76.4±61.4	392.10±762.1	-2.86	0.01
Alkaline phosphatase	181.5±95.8	361.31±301.09	-3.96	0.00
Coagulation parameters				
PT	16.6±7.9	61.10±69.80	-4.39	0.00
APTT	35.82±7.99	76.12±61.96	-4.47	0.00
INR	1.43±0.74	1.68±0.49	-1.85	0.07
BT	4.39±0.54	4.7±0.71	-2.71	0.01
CT	2.43±0.47	2.57±0.42	-1.49	0.14

Table 4: Comparison of alkaline phosphatase and serum albumin levels between dengue fever without warning signs and dengue fever with warning signs

Alk. Phosphatase & Ser. Albumin	Group 1 (n=48) Frequency (%)	Group 2 (n=52) Frequency (%)
Alkaline phosphatase levels (IU/L)		
<125	27.1	11.5
125-250	60.4	25.0
>250	12.5	63.5
Serum albumin levels (g/dL)		
2.0-2.4	10.4	34.6
2.5-2.9	14.6	32.7
3.0-3.4	37.5	26.9
>3.5	37.5	5.8

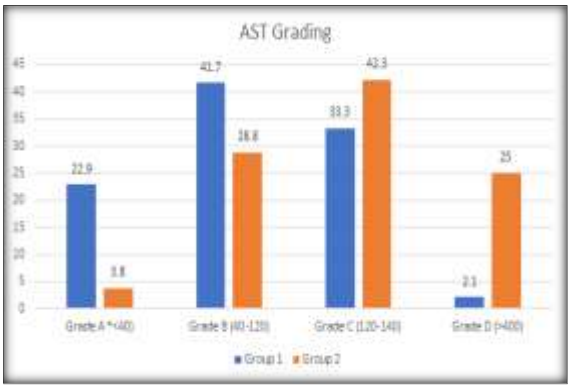

Figure 1: Comparison of AST levels between children with and without warning signs of dengue fever

DISCUSSION

This prospective observational study of 100 pediatric patients with serologically confirmed dengue fever revealed significantly greater hepatic dysfunction in children exhibiting warning signs compared to those without such signs. The elevation of aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin levels, and coagulation abnormalities indicates a significant correlation between hepatic involvement and the severity of dengue. The findings align with existing literature that recognizes liver injury as a significant predictor of disease progression in dengue infection.[8-10]

Elevated liver enzymes, specifically AST and ALT, are frequently observed in pediatric cases of dengue. Prior research indicated that elevated AST levels were observed in 38-94% of pediatric dengue cases, with increased levels associated with greater disease severity.[1] The consistently observed disproportionately higher rise of AST relative to ALT in dengue is regarded as characteristic of dengue-associated liver injury.[9-11] AST levels may rise significantly due to its release from skeletal muscle and erythrocytes during systemic inflammation or shock, conditions frequently observed in severe dengue.

Our study indicates that AST levels in children exhibiting warning signs (626.04±1253.5 U/L) were significantly elevated compared to those without warning signs (117.6±124.6 U/L). Multiple pediatric studies have documented similar trends, indicating that AST elevation serves as a more reliable indicator of severe disease compared to ALT.[13-14] This pattern has been elucidated through both direct viral cytopathic effects on hepatocytes and immune-mediated tissue damage.[9,10] In addition to hepatocellular injury, significant abnormalities were observed in bilirubin levels, serum albumin, and alkaline phosphatase. This indicates that dengue may

impact not only hepatocytes but also hepatic excretory and synthetic functions, particularly in patients exhibiting warning signs. Samanta and Sharma reported similar findings, demonstrating that dengue can induce a mixed pattern of hepatocellular and cholestatic injury.[10] The World Health Organization identifies liver involvement as a significant aspect of severe dengue, with multiple studies demonstrating that elevated transaminases are associated with the progression to dengue with warning signs (DWS).[13]

In our study, children in Group 2 (warning signs) exhibited significantly elevated levels of AST, ALT, bilirubin, ALP, and prolonged PT/aPTT values compared to Group 1 (without warning signs). The biochemical alterations corresponded with clinical manifestations including petechiae, melena, vomiting, abdominal pain, and icterus. Consistent reports have indicated similar associations between liver dysfunction and severe clinical signs.[13-15]

Hypoalbuminemia was noted at 2.70 ± 0.51 g/dL in Group 2 compared to 3.17 ± 0.52 g/dL in Group 1, and is established as an indicator of plasma leakage and severe dengue.[14] Decreased albumin levels may indicate impaired synthesis, heightened vascular permeability, or a combination of both factors, and are associated with negative outcomes including shock and haemorrhage.[14] The dengue virus, although not primarily targeting the liver, has the capacity to infect hepatocytes, Kupffer cells, and endothelial cells, leading to immune-mediated inflammation and apoptosis. In severe dengue, cytokine storm, capillary leakage, reduced hepatic perfusion, and microvascular dysfunction exacerbate liver injury.[10]

The elevated AST levels may indicate additional skeletal muscle injury during systemic inflammatory response or shock.[9,10] The elevation of bilirubin and the rise in alkaline phosphatase (ALP) in severe dengue may be attributed to intrahepatic cholestasis, hemolysis, or bile canalicular dysfunction, as indicated in previous studies.[10,11] This study highlights the significant correlation between liver dysfunction and warning signs, emphasizing the necessity of early liver function test assessment in pediatric dengue cases. Prior research has highlighted the clinical relevance of AST, ALT, albumin, and coagulation parameters in forecasting disease severity, length of hospitalization, and risk of bleeding.[10,13,14]

The findings indicate the necessity of including routine liver function and coagulation assessments, specifically AST, albumin, PT/aPTT, and bilirubin, in the initial evaluation of children with dengue, particularly in cases presenting with abdominal pain, persistent vomiting, bleeding tendencies, or hepatomegaly. Our findings are consistent with previous studies that report elevated transaminase levels in cases of severe dengue and dengue with warning signs.[8,12,13] Research indicates that AST elevation serves as a robust independent predictor of severe dengue, supporting our findings of significantly elevated AST levels in Group 2.[12] The elevation of AST/ALT in our cohort exceeds that observed in certain pediatric studies, where the mean AST typically remained below 200 U/L.[8] This may indicate regional variations in viral serotype distribution, differences in nutritional status, or discrepancies in the timing of sample collection.

Bilirubin elevation was notably significant in our warning-sign group, in contrast to earlier pediatric cohorts, which indicated jaundice in only a minor percentage of patients.[16] This indicates that hepatic involvement in our region may be more severe, potentially due to delayed presentation or environmental and genetic factors affecting host response.

This comparison between groups with warning signs and those without facilitates a significant interpretation of liver injury patterns. A thorough assessment of hepatic and coagulation markers enhances internal validity. This study is limited by a small number of participants, a lack of serial LFT measurements, and the absence of dengue serotype testing. Future research should incorporate larger sample sizes, continuous monitoring of liver enzymes, correlation with viral serotypes, and outcome-based stratification to determine prognostic cut-offs for severe disease.

CONCLUSION

In our prospective cohort of children with dengue fever, hepatic involvement was prevalent and notably more pronounced in those exhibiting warning signs. The warning-sign group exhibited a higher frequency of elevated AST and ALT, hyperbilirubinemia, hypoalbuminemia, elevated ALP, and coagulation derangement, indicating hepatic injury and compromised synthetic/excretory function in more severe disease cases. The findings align with existing literature and highlight the necessity of regular liver function monitoring in pediatric dengue, especially when warning signs are present, to facilitate early recognition, risk stratification, and prompt supportive care.

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