

## Original Research Article

# Atypical hepatic, cardiac, and renal manifestations in pediatric dengue: a prospective study

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## ABSTRACT

**Background:** Dengue fever is the most prevalent arboviral infection worldwide and is characterized by a broad clinical spectrum, ranging from self-limiting febrile illness to severe, life-threatening complications. In recent years, there has been growing recognition of atypical presentations, collectively referred to as expanded dengue syndrome (EDS), encompassing involvement of organs such as the liver, heart, and kidneys. The aim of this study was to evaluate the atypical hepatic, cardiac, and renal manifestations in children with dengue infection.

**Methods:** This prospective cohort study included 100 pediatric patients with serologically confirmed dengue infection. All participants underwent detailed clinical assessment along with laboratory investigations, including complete blood counts (CBC), liver function tests (LFT), renal function tests (RFT), coagulation profiles, and electrocardiographic (ECG) evaluation.

**Results:** The mean age of the study population was  $8.65 \pm 3.34$  years, with a slight male predominance (55%). Serological analysis showed that 72% of patients were positive for NS1 antigen alone, whereas 28% demonstrated both NS1 and IgM positivity. Hepatic involvement was common, with elevated SGOT levels observed in 51% of cases, while SGPT elevation was noted in only 6%. Hematological abnormalities were prominent, with anemia detected in 93% and thrombocytopenia in 86% of patients. Renal involvement was relatively infrequent; elevated serum creatinine was seen in 9% of cases, and proteinuria in 1%. No electrocardiographic abnormalities were identified in the study cohort. On subgroup analysis, patients with combined NS1 and IgM positivity had significantly lower platelet counts ( $p=0.0397$ ) and hemoglobin levels ( $p<0.0001$ ) compared to those with isolated NS1 positivity.

**Conclusions:** Hepatic transaminitis and hematological cytopenias constitute common systemic manifestations, with occasional atypical involvement in pediatric dengue. Concurrent positivity for NS1 antigen and IgM antibody is associated with a more severe clinical profile, suggesting its potential role as a marker of disease severity.

**Keywords:** Dengue, Expanded dengue syndrome, Hepatic dysfunction, Pediatric dengue, Acute kidney injury, Myocarditis

## INTRODUCTION

Dengue fever is a major global health issue, particularly in tropical and subtropical regions, and has seen a rapid increase in incidence. While the majority of dengue virus infections are asymptomatic or present with mild febrile symptoms, the disease can rapidly progress to severe dengue, dengue hemorrhagic fever (DHF), or dengue shock syndrome (DSS).<sup>1-4</sup>

Increasingly, dengue is recognized as a multifaceted systemic disease capable of inducing EDS.<sup>2</sup> EDS encompasses atypical manifestations involving multiple organ systems, resulting in complications such as acute liver failure, myocarditis, and acute kidney injury. Liver injury is particularly common and can result from direct viral toxicity or dysregulated immunologic responses.<sup>3-5</sup> Despite the growing burden of these complications, studies focusing specifically on atypical manifestations in

the pediatric population remain limited.<sup>5</sup> This study aims to evaluate the hepatic, cardiac, and renal manifestations of dengue in children aged 1 to 16 years.

## METHODS

### *Study design and setting*

This prospective cohort study was conducted in the Department of Pediatrics at Navodaya Medical College Hospital and Research Centre over a period of 18 months.

### *Participants*

A total of 100 children aged 1 to 16 years, admitted with a diagnosis of dengue fever, were enrolled in the study.

Inclusion was restricted to serologically confirmed cases, defined by positivity for NS1 antigen and/or dengue-specific IgM or IgG antibodies, along with compatible clinical features. Children with pre-existing congenital or acquired cardiac disease, as well as those with concurrent infections such as malaria, enteric fever, or viral hepatitis, were excluded to minimize confounding.

### *Data collection and investigations*

Ethical approval was obtained from the institutional ethics committee before starting the data collection.

Data were collected using a predesigned proforma following written informed parental consent. All patients underwent detailed clinical evaluation and standard laboratory investigations, including CBC, LFT, RFT, prothrombin time, and international normalized ratio. Anemia was defined as per WHO age-specific hemoglobin cutoffs. Assessment for atypical manifestations was performed using targeted investigations, including electrocardiography, echocardiography, and abdominal ultrasonography.

### *Statistical analysis*

Data were analyzed using SPSS software (version 26.0; IBM SPSS statistics). Continuous variables were compared using independent sample t test/Mann-Whitney U test. Categorical variables were analyzed using the chi-square test.  $P \leq 0.05$  considered statistically significant.

## RESULTS

### *Baseline demographic and serological profile of study participants*

#### *Demographic profile*

The mean age of the study population was  $8.65 \pm 3.34$  years, with nearly half of the participants (47%) belonging to the 6-10-year age group. There was a slight

male predominance, with males accounting for 55% of cases (Table 1).

#### *Dengue serology*

Serological evaluation showed that 72% of patients were positive for NS1 antigen alone, while the remaining 28% demonstrated both NS1 antigen and IgM antibody positivity.

### *Hematological, hepatic, renal, and cardiac profile of study population*

#### *Hematological findings*

Hematological abnormalities were prominent across the cohort. Anemia was observed in 93% of patients. Thrombocytopenia (platelet count  $< 1.5$  lakh cells/mm<sup>3</sup>) was present in 86%, with a mean platelet count of  $1.05 \pm 0.45$  lakh cells/mm<sup>3</sup>.

Leukopenia (total leukocyte count  $< 4000$  cells/mm<sup>3</sup>) was noted in 18% of cases (Table 2).

#### *Hepatic manifestations*

Hepatic involvement was largely subclinical and identified primarily through biochemical derangements. Elevated SGOT levels were seen in 51% of patients, with a mean value of  $60.32 \pm 30.88$  U/l. In contrast, SGPT elevation was less frequent, observed in only 6% of cases (mean  $33.30 \pm 9.62$  U/l). Coagulation abnormalities were uncommon, with prolonged prothrombin time and international normalized ratio observed in 1% and 5% of patients, respectively.

#### *Renal and cardiac manifestations*

Renal involvement was relatively infrequent. Elevated serum creatinine was observed in 9% of patients (mean  $0.37 \pm 0.35$  mg/dl). Proteinuria (1+) was detected in a single patient (1%), while hematuria was not observed. Cardiac evaluation revealed no electrocardiographic abnormalities.

### *Association between dengue seropositivity and clinical parameters*

#### *Correlation with disease severity*

Comparative analysis between patients with isolated NS1 positivity and those with combined NS1 and IgM positivity revealed significant differences.

The dual-positive group had lower mean platelet counts ( $90,264$  vs.  $110,918$  cells/mm<sup>3</sup>;  $p=0.0397$ ) and reduced hemoglobin levels ( $9.46$  vs.  $9.87$  g/dl;  $p<0.0001$ ). While differences in coagulation parameters were not statistically significant (Table 3).

**Table 1: Baseline demographic and serological profile of study participants.**

| Variables                                  | Category           | Total, (n=100) | Percentage (%) |
|--|--------------------|----------------|----------------|
| <b>Age (in years) (Mean±SD: 8.65±3.34)</b> | <5                 | 20             | 20             |
|  | 6-10               | 47             | 47             |
|  | 11-16              | 33             | 33             |
| <b>Gender</b>                              | Male               | 55             | 55             |
|  | Female             | 45             | 45             |
| <b>Dengue serology</b>                     | NS1 positive       | 72             | 72             |
|  | NS1 + IgM positive | 28             | 28             |

**Table 2: Hematological, hepatic, renal, and cardiac profile of study population.**

| Parameters                   | Units                      | Categories                                      | Distribution (%) | Mean±SD         |
|------------------------------|----------------------------|---|------------------|-----------------|
| <b>WBC</b>                   | cells/mm <sup>3</sup>      | Leukopenia (<4000)/normal/leukocytosis (>11000) | 18/76/6          | 6589.30±2679.90 |
| <b>Platelets</b>             | Lakh cells/mm <sup>3</sup> | Thrombocytopenia (<1.5)/normal                  | 86/14            | 1.05±0.45       |
| <b>Hemoglobin</b>            | g/dl                       | Anemia/normal                                   | 93/7             | 9.76±1.61       |
| <b>SGOT</b>                  | U/l                        | Normal/elevated                                 | 49/51            | 60.32±30.88     |
| <b>SGPT</b>                  | U/l                        | Normal/elevated                                 | 94/6             | 33.30±9.62      |
| <b>Prothrombin time (PT)</b> | seconds                    | Normal/prolonged                                | 99/1             | 12.20±0.83      |
| <b>INR</b>                   | -                          | Normal/elevated                                 | 95/5             | 0.98±0.13       |
| <b>Serum creatinine</b>      | mg/dl                      | Normal/elevated                                 | 91/9             | 0.37±0.35       |
| <b>Proteinuria (≥1+)</b>     | -                          | Present/absent                                  | 1/99             | -               |
| <b>Hematuria</b>             | -                          | Present/absent                                  | 0/100            | -               |
| <b>ECG abnormalities</b>     | -                          | Present/absent                                  | 0/100            | -               |

**Table 3: Association between dengue seropositivity and clinical parameters.**

| Parameters                                   | NS1 positive (n=72), mean±SD | NS1 + IgM positive (n=28), mean±SD | P value |
|--|------------------------------|------------------------------------|---------|
| <b>WBC count (cells/mm<sup>3</sup>)</b>      | 6911.53±2477.75              | 5760.71±2984.88                    | 0.052   |
| <b>Platelet count (cells/mm<sup>3</sup>)</b> | 110918.10±43716.89           | 90264.29±46462.28                  | 0.0397  |
| <b>Hemoglobin (g/dL)</b>                     | 9.87±1.60                    | 9.46±1.58                          | <0.0001 |
| <b>Prothrombin time (seconds)</b>            | 12.16±0.76                   | 12.22±0.98                         | 0.926   |
| <b>INR</b>                                   | 0.98±0.12                    | 1.01±0.13                          | 0.842   |

\*p<0.05 considered statistically significant.

## DISCUSSION

Dengue infection is a systemic illness with the potential to cause multiorgan involvement, driven by a combination of plasma leakage, tissue hypoperfusion, and an exaggerated host immune response.<sup>7,8</sup> In the present cohort, hematological abnormalities were particularly prominent, with thrombocytopenia (86%) and anemia (93%) observed in the majority of patients, underscoring the significant hematopoietic impact of the infection. The high prevalence of anemia may reflect underlying nutritional deficiency in the study population.

Hepatic involvement was a consistent finding and largely mirrored patterns described in existing literature.<sup>11-14</sup> Elevated SGOT levels (51%) were considerably more frequent than SGPT elevations (6%). This disproportionate rise in the aspartate aminotransferase

compared to alanine aminotransferase has been widely reported in dengue and is often attributed not only to hepatic injury but also to extrahepatic sources, particularly skeletal muscle involvement.<sup>16</sup>

In contrast, renal and cardiac manifestations were relatively uncommon in this study population. Elevated serum creatinine was observed in a small proportion of patients (9%), while electrocardiographic abnormalities were not detected. These findings suggest that although renal and cardiac complications are recognized components of EDS, their occurrence may be limited in uncomplicated cases and tends to be more closely associated with severe disease, particularly dengue shock syndrome.<sup>19-22</sup>

A notable observation in this study was the association between dual seropositivity (NS1 antigen and IgM

antibody) and increased disease severity. This may represent a transitional phase associated with increased disease activity. Patients with combined positivity demonstrated lower platelet counts, and reduced hemoglobin levels. This pattern may reflect a critical phase in the disease course, wherein ongoing viremia coincides with an evolving immune response, leading to enhanced endothelial dysfunction and hematological compromise.<sup>6</sup>

### Limitations

This was a single-center study with a relatively small sample size, which may limit generalizability. Cardiac and renal assessments were based on routine investigations, and subclinical involvement may have been missed. The study did not stratify patients according to standard dengue severity classifications, limiting correlation with disease severity. Additionally, the high prevalence of anemia may reflect underlying nutritional deficiencies rather than dengue alone.

### CONCLUSION

In pediatric dengue, atypical hepatic involvement is common, most frequently manifesting as elevated SGOT levels, and is often accompanied by significant hematological abnormalities, particularly thrombocytopenia and anemia. Renal and cardiac complications, although potentially severe, were infrequent in this cohort.

Notably, concurrent positivity for NS1 antigen and IgM antibody was associated with a more severe clinical profile, indicating its potential utility as a marker of disease severity. Recognition of this subgroup may facilitate early risk stratification and guide closer monitoring with timely supportive interventions.

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