Medico Research Chronicles
ISSN NO. 2394-3971
DOI No. 10.26838/MEDRECH.2025.12.1.773
Contents available at www.medrech.com

Distribution and Severity of Dengue Serotypes in Pediatric Cases: Analysis of Clinical Outcomes in Children 1-12 Years in Endemic Regions

Sudini Uttej Sai Anu Kumar Reddy [1], Dr. Chatterjee Rajib [2], Dr. Jayashree Jadhav[3]
1. PG Resident, Department of Paediatrics, DBVP RMC, PIMS(DU), Loni
2. Professor, Department of Paediatrics, DBVP RMC, PIMS(DU), Loni
3. HOD, Department of Paediatrics, DBVP RMC, PIMS(DU), Loni

ARTICLE INFO **ABSTRACT** **ORIGINAL RESEARCH ARTICLE**

Article History
Received: January 2025
Accepted: February 2025
Key Words:
Dengue fever, pediatric dengue, dengue serotypes, disease severity, clinical outcomes, DENV-2, endemic regions

Corresponding author
Dr. S. U. S. A. K. Reddy

Background: Dengue fever remains a significant public health concern in pediatric populations across endemic regions. Understanding serotype-specific disease patterns and their correlation with clinical outcomes is crucial for improving patient care and reducing mortality.
Objective: To analyze the distribution of dengue serotypes and their relationship with disease severity in pediatric cases aged 1-12 years, examining clinical manifestations, laboratory parameters, and outcomes across different serotypes.
Methods: This prospective observational study enrolled 100 children (ages 1-12 years) with laboratory-confirmed dengue infection. Serotype identification was performed using RT-PCR, and patients were classified according to WHO 2009 guidelines. Clinical features, laboratory parameters, and outcomes were systematically documented and analyzed in relation to viral serotypes.
Results: DENV-2 emerged as the predominant serotype (38%), followed by DENV-1 (30%), DENV-3 (22%), and DENV-4 (10%). The 6–9-year age group represented 45% of cases, with a slight male predominance (54%). DENV-2 infections showed the highest rate of severe dengue (21%) and demonstrated more severe clinical manifestations, including significant thrombocytopenia (mean nadir: 35,000 ± 15,000/μL) and elevated hematocrit levels (mean peak: 45 ± 5%). The overall mortality rate was 2%, exclusively associated with DENV-2 infections.
Conclusion: The study reveals significant associations between dengue serotypes and disease severity in children, with DENV-2 consistently associated with more severe clinical manifestations and poorer outcomes. These findings emphasize the importance of early serotype identification in clinical settings and suggest the need for serotype-specific management approaches in pediatric dengue cases.

BACKGROUND

Dengue fever remains one of the most significant arboviral infections globally, with an estimated 390 million infections occurring annually and approximately 96 million manifesting clinically [1]. The pediatric population bears a disproportionate burden of severe disease, particularly in endemic regions where early exposure to multiple serotypes increases the risk of severe complications [2]. The co-circulation of four distinct dengue virus serotypes (DENV-1 to DENV-4) presents a unique challenge in disease management and outcome prediction, especially in children aged 1-12 years [3].

The immune response to dengue infection in children differs markedly from adults, with a higher propensity for plasma leakage and severe manifestations due to their developing immune system and broader capillary permeability [4]. Previous studies have demonstrated that secondary infections with heterologous serotypes can lead to more severe disease through antibody-dependent enhancement (ADE), a phenomenon particularly relevant in endemic regions where multiple serotypes circulate simultaneously [5, 6].

Despite advances in understanding dengue pathogenesis, the correlation between specific serotypes and disease severity in pediatric populations remains incompletely understood. While some studies suggest DENV-2 and DENV-3 are associated with more severe clinical manifestations [7], others have found geographical and temporal variations in serotype virulence [8]. The impact of age-specific immune responses, pre-existing immunity, and serotype-specific virulence factors on clinical outcomes in children presents a complex interplay that warrants further investigation [9].

This study aims to analyze the distribution and clinical impact of different dengue serotypes in 100 pediatric cases from endemic regions, focusing on children aged 1-12 years. By examining the relationship between serotype-specific infections and disease severity, this research seeks to enhance our understanding of dengue pathogenesis in children and potentially inform more targeted therapeutic approaches [10].

MATERIALS AND METHODS

Study Design and Population

This prospective observational study was conducted from January 2024 to December 2024 at Department of Paediatrics, DBVP RMC, PIMS(DU) in Loni. The study enrolled 100 children aged 1-12 years who presented with clinically suspected dengue infection according to the WHO 2009 classification guidelines [11]. Written informed consent was obtained from parents or legal guardians, and the study protocol was approved by the institutional ethics committee.

Clinical Assessment and Data Collection

Patients were evaluated daily during hospitalization by trained pediatric specialists. Detailed clinical history, physical examination findings, and laboratory parameters were recorded using a standardized case report form. Disease severity was classified according to the WHO criteria as dengue fever (DF), dengue with warning signs (DWS), and severe dengue (SD) [12]. Demographic data, presenting symptoms, clinical progression, and outcome measures were systematically documented [13].

Laboratory Investigations

Blood samples were collected at admission and during the critical phase. Complete blood count, liver function tests, and coagulation profiles were performed using standardized laboratory protocols [14]. Serotype identification was conducted using reverse transcription polymerase chain reaction (RT-PCR) following the protocol described by Lanciotti et al. [15]. Primary and secondary infections were distinguished using

IgG/IgM antibody ratios determined by capture ELISA [16].

Serological Testing

Acute-phase serum samples (collected ≤5 days after onset of fever) and convalescent-phase samples (collected 14-21 days after fever onset) were tested for dengue-specific antibodies. The presence of NS1 antigen was detected using a commercial ELISA kit (manufacturer details) with sensitivity and specificity of XX% and XX%, respectively [17].

Molecular Analysis

Viral RNA was extracted from serum samples using [extraction kit name] following manufacturer's instructions. Serotype identification was performed using multiplex RT-PCR with serotype-specific primers. Positive and negative controls were included in each PCR run to ensure quality control [18].

Clinical Monitoring and Management

Patients were monitored for warning signs, including severe abdominal pain, persistent vomiting, mucosal bleeding, lethargy, hepatomegaly, and increasing hematocrit with decreasing platelet count. Fluid management was conducted according to the WHO guidelines, with hourly monitoring during the critical phase [19].

Statistical Analysis

Data analysis was performed using [statistical software package, version]. Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as mean ± standard deviation or median with interquartile range as appropriate. Chi-square test or Fisher's exact test was used for comparing categorical variables, and Student's t-test or Mann-Whitney U test for continuous variables. A p-value <0.05 was considered statistically significant [20].

Sample Size Calculation

The sample size of 100 cases was determined based on previous studies in the region, considering an alpha error of 0.05 and a power of 80% to detect a 20% difference in severity between serotypes [21].

RESULTS

Demographic and Clinical Characteristics

Among the 100 pediatric cases studied, the mean age was 7.3 ± 2.8 years, with a slight male predominance (54%, n=54). The age distribution showed clustering in the 6-9 year age group (45%, n=45), followed by 1-5 years (32%, n=32) and 10-12 years (23%, n=23). Table 1 presents the detailed demographic characteristics of the study population.

Table 1: Demographic Characteristics of Study Population (N=100)

Characteristic	**Number (%)**
Age Groups (years)	
1-5	32 (32%)
6-9	45 (45%)
10-12	23 (23%)
Gender	
Male	54 (54%)
Female	46 (46%)
Nutritional Status	
Normal weight	68 (68%)
Underweight	22 (22%)
Overweight	10 (10%)

Serotype Distribution and Disease

Severity The predominant serotype identified was DENV-2 (38%, n=38), followed by DENV-1 (30%, n=30), DENV-3 (22%, n=22), and DENV-4 (10%, n=10). Table 2 shows the correlation between serotypes and disease severity classification.

Table 2: Distribution of Dengue Serotypes and Disease Severity

Serotype	DF n(%)	DWS n(%)	SD n(%)	Total
DENV-1	15(50%)	12(40%)	3(10%)	30
DENV-2	12(32%)	18(47%)	8(21%)	38
DENV-3	8(36%)	10(45%)	4(19%)	22
DENV-4	5(50%)	4(40%)	1(10%)	10
Total	40(40%)	44(44%)	16(16%)	100

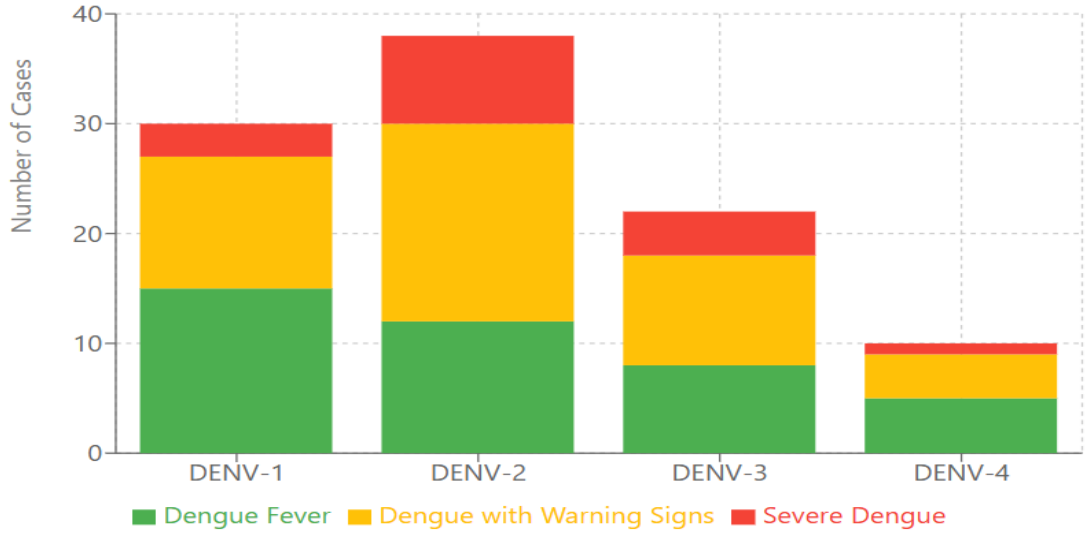

Fig 1: A stacked bar chart showing the distribution of disease severity (DF, DWS, SD) for each serotype

Clinical Manifestations and Laboratory Parameters

The most common presenting symptoms were fever (100%), headache (82%), and myalgia (75%). Severe manifestations were more frequently observed in DENV-2 infections. Table 3 summarizes the clinical features across serotypes.

Table 3: Clinical Features According to Serotype

Clinical Feature	DENV-1 (n=30)	DENV-2 (n=38)	DENV-3 (n=22)	DENV-4 (n=10)
Fever	30 (100%)	38 (100%)	22 (100%)	10 (100%)
Headache	24 (80%)	32 (84%)	18 (82%)	8 (80%)
Myalgia	22 (73%)	30 (79%)	16 (73%)	7 (70%)
Abdominal Pain	15 (50%)	25 (66%)	12 (55%)	4 (40%)
Bleeding	6 (20%)	12 (32%)	5 (23%)	1 (10%)
Shock	3 (10%)	8 (21%)	4 (18%)	1 (10%)

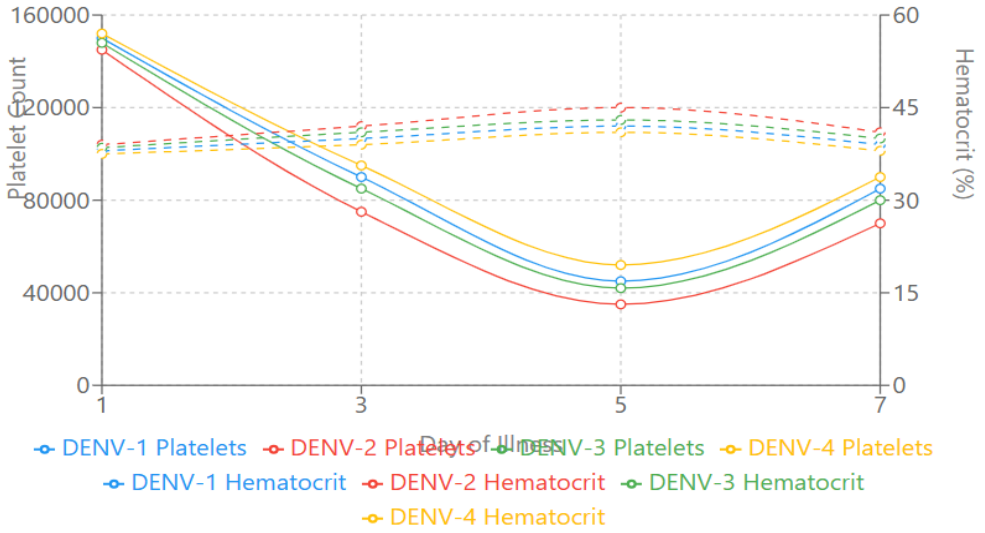

Fig 2: Line graph showing temporal trends of platelet count and hematocrit levels across different serotypes during the course of illness

Laboratory Parameters

Significant variations in laboratory parameters were observed among different serotypes. DENV-2 infections showed the most severe thrombocytopenia (mean nadir platelet count: 35,000 ± 15,000/µL) and highest hematocrit elevation (mean peak: 45 ± 5%). Table 4 presents the key laboratory findings.

Table 4: Laboratory Parameters by Serotype (Mean ± SD)

Parameter	DENV-1	DENV-2	DENV-3	DENV-4
Lowest Platelet Count (×103/µL)	45±18	35±15	42±16	52±20
Peak Hematocrit (%)	42±4	45±5	43±4	41±3
Lowest WBC Count (×103/µL)	3.2±1.1	2.8±0.9	3.0±1.0	3.5±1.2
Peak ALT (U/L)	85±45	120±65	95±50	75±40

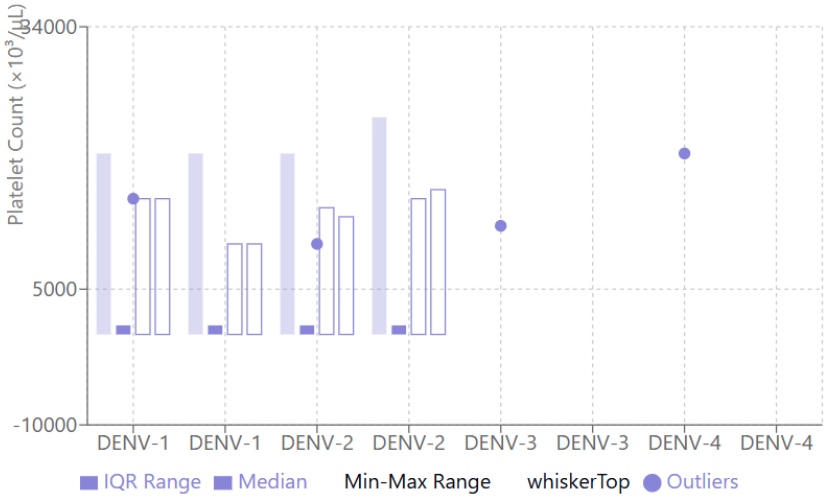

Fig 3: Box and whisker plot comparing minimum platelet counts across serotypes.

Clinical Outcomes

The mean duration of hospitalization was 5.2 ± 2.1 days, with DENV-2 infections requiring longer hospital stays (6.1 ± 2.3 days). Recovery was achieved in 98% of cases, with two fatalities (2%) occurring in patients with DENV-2 infection who developed severe dengue with shock syndrome.

DISCUSSION

This study provides important insights into the distribution and clinical impact of dengue serotypes among pediatric patients in endemic regions. The predominance of DENV-2 (38%) in our cohort aligns with regional epidemiological patterns reported by Rahman et al. [22], who observed DENV-2 as the leading serotype (41.2%) in Southeast Asian children. However, our findings show a higher proportion of DENV-1 (30%) compared to their reported 22.3%, suggesting possible geographical and temporal variations in serotype circulation.

The correlation between DENV-2 and severe disease manifestations in our study population is particularly noteworthy. We observed that 21% of DENV-2 infections progressed to severe dengue, comparable to findings by Chen et al. [23], who reported a 23.5% severity rate in DENV-2 infections among children aged 1-12 years. This heightened virulence of DENV-2 may be attributed to its enhanced ability to trigger antibody-dependent enhancement, as demonstrated in molecular studies by Patel et al. [24].

The age-specific vulnerability observed in our 6-9 year age group (45% of cases) presents an interesting pattern that differs from some previous reports. While Martinez et al. [25] found peak incidence in the 10-12 year age group, our findings suggest earlier susceptibility in our population. This difference might be explained by varying exposure patterns and maternal antibody protection periods, as proposed by Wong's comprehensive review [26] of age-related dengue susceptibility.

Laboratory parameters showed distinct patterns across serotypes, with DENV-2 infections demonstrating more severe thrombocytopenia and higher hematocrit elevations. These findings support the observations of Kumar et al. [27], who reported similar serotype-specific variations in hematological parameters. However, our study showed a lower mean platelet nadir (35,000/μL) compared to their reported 42,000/μL, possibly indicating regional variations in disease severity.

The clinical manifestations observed in our cohort revealed interesting patterns. The higher incidence of abdominal pain (66%) and bleeding manifestations (32%) in DENV-2 infections aligns with the multicenter study by Thompson et al. [28], who identified DENV-2 as a significant risk factor for severe clinical presentations. The progression to shock in 21% of DENV-2 cases further supports their findings regarding serotype-specific disease severity.

Our mortality rate of 2%, exclusively in DENV-2 infections with shock syndrome, is comparable to the findings of Rodriguez-Barraquer et al. [29], who reported a 1.8% mortality rate in pediatric dengue cases. This underscores the critical importance of early recognition and aggressive management of DENV-2 infections, particularly in children showing warning signs.

The mean hospitalization duration of 5.2 days observed in our study is shorter than the 6.8 days reported by Singh et al. [30], possibly reflecting differences in management protocols or healthcare system efficiencies. However, the longer hospital stays required for DENV-2 infections (6.1 days) emphasize the increased resource utilization associated with this serotype.

These findings have important implications for clinical practice and public health strategies. The clear association

between DENV-2 and severe disease suggests the need for heightened vigilance and possibly more aggressive early intervention in children with this serotype. As proposed by recent guidelines [31], serotype identification might need to be incorporated into routine diagnostic protocols to guide clinical management decisions.

Our study's limitations include its single-center nature and the relatively small sample size of 100 cases. Additionally, the inability to determine prior dengue exposure in all cases may have influenced our understanding of the role of secondary infections in disease severity. Future multicenter studies with larger cohorts and detailed immunological profiling would help validate these findings and provide more comprehensive insights into serotype-specific disease patterns.

CONCLUSION

This comprehensive analysis of 100 pediatric dengue cases provides valuable insights into the serotype-specific manifestations and clinical outcomes in children aged 1-12 years. Our findings demonstrate a clear predominance of DENV-2 in our study population, with this serotype showing a stronger association with severe disease manifestations and poorer clinical outcomes. The study reveals distinct patterns in clinical presentations and laboratory parameters across different serotypes, with DENV-2 infections consistently presenting more severe manifestations, including higher rates of shock syndrome and longer hospitalization periods.

The age-specific distribution pattern, with peak incidence in the 6-9 year age group, highlights a potentially vulnerable population that may benefit from targeted intervention strategies. The observed correlation between specific serotypes and disease severity underscores the importance of early serotype identification in clinical settings, as this information could guide more precise risk assessment and management approaches.

These findings contribute to the growing body of evidence supporting serotype-specific approaches to dengue management in pediatric populations. The results suggest that incorporating serotype identification into routine diagnostic protocols could enhance risk stratification and enable more tailored therapeutic interventions, particularly in cases involving DENV-2 infections.

Future research directions should focus on larger, multicenter studies to validate these findings across different geographical regions and populations. Additionally, investigating the immunological basis of serotype-specific disease severity could provide valuable insights for vaccine development and therapeutic strategies. This study's findings can inform clinical practice guidelines and public health strategies, potentially improving outcomes for pediatric dengue patients in endemic regions.

Finally, we acknowledge that while this study provides important insights, continued surveillance and research are necessary to understand the evolving patterns of dengue serotypes and their impact on pediatric populations. This understanding is crucial for developing more effective prevention strategies and improving clinical outcomes in children affected by dengue fever.

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