Research Article

Clinical, Hematological, Biochemical And Serotype Correlates Of Disease Severity In Hospitalized Dengue Patients: A Cross-Sectional Study Of 100 Patients

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Abstract

Background: Dengue infection exhibits a broad clinical spectrum, and early recognition of patients at risk of severe disease remains important. This study evaluated the relationship of routine hematological and biochemical parameters with clinical manifestations, described dengue virus serotype distribution, and examined associations between serotype patterns and disease severity in hospitalized patients.

Materials and methods: The study was conducted in Department of Microbiology of Jaipur National University Instruction of Medical Science and Research Center, Jaipur, Rajasthan. This study included 100 patients aged >11 years with laboratory confirmed dengue and platelet counts below 100,000/µL. Demographic, clinical, hematological, biochemical, serological, molecular serotype were analyzed. Severe and non-severe dengue were compared using non-parametric tests for continuous variables and chi-square/Fisher's exact tests for categorical variables. Spearman rank correlation was used for exploratory assessment of laboratory parameters and clinical-manifestation burden.

Results Data of 100 patients were analyzed, where 57 were female and 43 male; the median age was 27 years (IQR 21–37). Nineteen patients (19%) were classified as severe dengue and 81 (81%) as non-severe. The most frequent manifestations were fever (97%), abdominal pain (92%), arthralgia (90%), prostration (90%), myalgia (89%), headache (88%) and hepatomegaly (84%). Median laboratory values did not differ significantly between severe and non-severe groups for hemoglobin, TLC, MCV, hematocrit, platelet count, INR, bilirubin, AST, ALT, total protein, albumin, creatinine or urea (all $p>0.05$). DENV-2 was the most frequent single serotype (33%), followed by DENV-3 (28%), DENV-1 (13%) and DENV-4 (9%); mixed-serotype infections accounted for 17%. Mixed infections were strongly associated with severe dengue (10/17 [58.8%] severe versus 9/83 [10.8%] among single-serotype infections; Fisher's exact $p<0.001$). DENV-2+DENV-3 infection was particularly associated with severe disease (6/9 [66.7%], $p=0.0013$).

Conclusion: The study demonstrates substantial clinical heterogeneity and co-circulation of all four dengue serotypes. Although routine laboratory parameters were not statistically different between severity groups in this dataset, mixed-serotype infection especially DENV-2+DENV-3 was associated with a markedly higher proportion of severe disease. Molecular serotyping together with systematic clinical and laboratory monitoring may improve risk stratification.

Keywords: DENV serotypes, severe dengue, thrombocytopenia, hematological parameters; biochemical parameters; RT-PC.

1. Introduction

Dengue is a major mosquito borne viral infection in tropical and subtropical regions and remains an important public health problem in India. The virus comprises four antigenically distinct serotypes, DENV 1 to DENV 4 and the relative circulation of these serotypes varies geographically and temporally. Indian epidemiological evidence has demonstrated substantial regional variation and co-circulation of multiple serotypes, emphasizing the value of continued molecular surveillance (Ganeshkumar et al., 2018; Deshpande et al., 2026).

Clinical disease ranges from dengue without warning signs to dengue with warning signs and severe dengue. The WHO classification identifies severe plasma leakage, severe bleeding and severe organ involvement as principal pathways to severe disease (World Health Organization [WHO], 2009). Common warning signs include abdominal pain, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy or restlessness, hepatomegaly, and a rise in hematocrit accompanied by a rapid decrease in platelet count. Clinical predictors and laboratory abnormalities such as thrombocytopenia, hematocrit changes, hypoalbuminemia and elevated aminotransferases

have been associated with progression to severe disease in previous studies (Sangkaew et al., 2021; Tsheten et al., 2021; Huy & Toàn, 2022).

Serotype specific differences in disease severity remain an area of active investigation. Earlier hospital based Indian studies reported differences in clinical manifestations and liver enzyme abnormalities across serotypes, while meta analytic evidence suggests that the relationship between serotype and severity may depend on geographic region, primary versus secondary infection and host factors (Kumaria, 2010; Soo et al., 2016). Recent Indian surveillance studies continue to show DENV-2 predominance in several settings and indicate that concurrent infections may be associated with thrombocytopenia and hemorrhagic manifestations (Deshpande et al., 2026; Patil et al., 2026).

The present study was designed to integrate clinical manifestations with routine hematological and biochemical investigations and molecular serotype data in a defined hospital cohort. This approach may help clarify the clinical and laboratory characteristics of severe dengue and determine whether specific serotype patterns are associated with disease severity.

2. Material and Method

2.1 Study Design and Setting

This cross-sectional observational study was conducted among patients attending the tertiary care center at the Jaipur National University Institute of Medical Sciences and Research Centre, Jaipur, Rajasthan.

2.2 Inclusion Criteria

Age >11 years.

Hospitalized patients with laboratory-confirmed dengue infection based on the diagnostic testing recorded in the study dataset.

Platelet count <100,000/µL.

2.3 Exclusion

Patients aged ≤11 years.

Patients with incomplete records preventing classification of disease severity.

Patients with documented chronic hepatic, renal, hematological or malignant disorders likely to substantially alter the laboratory parameters under study.

Patients with another confirmed acute febrile infection or major concurrent infection that could confound the clinical/laboratory assessment.

2.4 Clinical and laboratory variables

Clinical variables included fever, headache, vomiting, abdominal pain, myalgia, arthralgia, retro orbital pain, prostration, rash, neck stiffness, sore throat, melena, spontaneous bleeding, gastrointestinal symptoms, hepatomegaly, splenomegaly, breathing difficulty, pleural effusion and bleeding manifestations. Hematological variables included hemoglobin, TLC, MCV, hematocrit, platelet count, PT and INR. Biochemical variables included total bilirubin, AST/SGOT, ALT/SGPT, total protein, albumin, serum creatinine and serum urea. Serological variables included NS1, IgM and IgG markers, while molecular fields recorded DENV-1, DENV-2, DENV-3 and DENV-4 and the final serotype pattern.

2.5 Molecular serotyping

Serotype results were analyzed according to the molecular detection fields recorded in the dataset. Serotype patterns were classified as single-serotype infection (DENV-1, DENV-2, DENV-3 or DENV-4) or mixed-serotype infection (e.g., DENV-2+DENV-3).

2.6 Disease severity and outcomes

Disease severity was analyzed using the severity classification recorded in the study dataset and dichotomized into non-severe and severe dengue for the principal comparison. The dataset contained 81 non-severe and 19 severe cases.

2.7 Statistical analysis

Statistical analysis followed a standard SPSS-compatible workflow. Categorical variables were summarized as frequencies and percentages. Continuous variables were summarized using the median and interquartile range (IQR) because of non-normal distributions and the presence of extreme recorded values. The Mann Whitney U test was used to compare continuous laboratory parameters between severe and non-severe dengue. Associations between

categorical variables were examined using Pearson's chi-square test or Fisher's exact test when expected cell counts were small. Spearman rank correlation was used to explore associations between laboratory parameters and the overall clinical manifestation burden. Two-sided p values <0.05 were considered statistically significant.

3. Result

Among the 100 patients, 57 (57.0%) were female and 43 (43.0%) were male (Fig 1). The median age was 27 years (IQR 21–37; range 13–76 among 99 patients with recorded age). The largest age group was 21–30 years (39%), followed by 11–20 years (23%) and 31–40 years (15%). Severe dengue was recorded in 19 patients (19%), while 81 (81%) were classified as non-severe.

Age group was associated with severity (χ^2 p=0.0075), with the proportion of severe dengue increasing from 4.3% in the 11–20-year group to 60.0% among patients older than 60 years. Sex was not significantly associated with severity (χ^2 p=0.390). (Table1)

Table 1. Demographic Characteristics and Disease Severity

Sex	**N=100**	**Percent**
Female	57	57.0%
Male	43	43.0%
Age group		
11–20 years	23	23.0%
21–30 years	39	39.0%
31–40 years	15	15.0%
41–50 years	8	8.0%
51–60 years	10	10.0%
>60 years	5	5.0%
Severity		
Non severe	81	81.0%
Severe	19	19.0%

Figure 1. Age-group distribution of the 100 dengue patients.

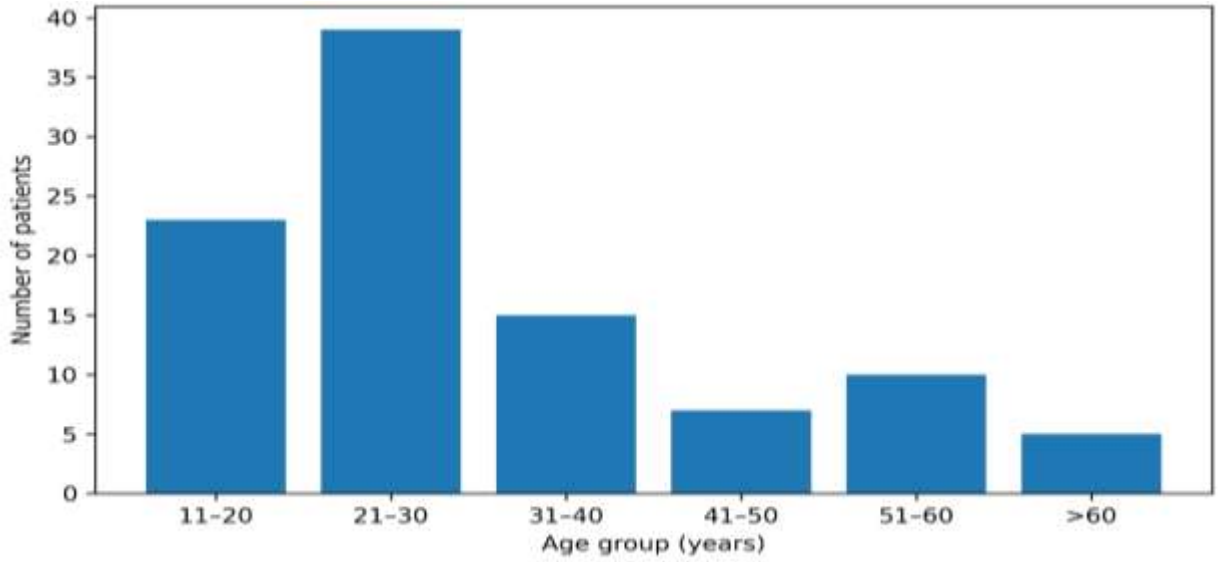
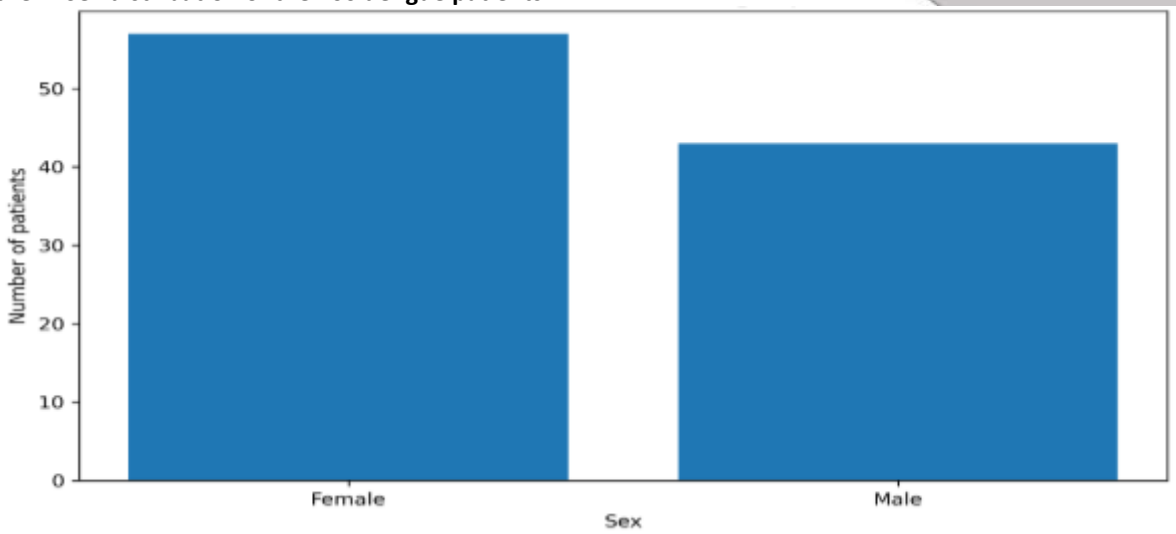


Figure 2. Sex distribution of the 100 dengue patients.



Clinical manifestations and disease severity

The most frequent manifestations were fever (97%), abdominal pain (92%), arthralgia (90%), prostration (90%), myalgia (89%), headache (88%) and hepatomegaly (84%). Fever and abdominal pain were present in 94.7% of severe cases, while vomiting occurred in 84.2% of severe cases. None of the individual manifestations reached statistical significance in the severe versus non-severe comparison in this sample (all p>0.05), although several manifestations showed clinically relevant differences in frequency. (Table 2)

Table 2. Clinical Manifestations According to Disease Severity

Clinical manifestation	Non-severe		Severe		
	N = 81	Percent	N = 19	Percent	p-value
Fever	79	97.5	18	94.7	0.472
Headache	71	87.7	17	89.5	1.000
Vomiting	61	75.3	16	84.2	0.553
Abdominal pain	74	91.4	18	94.7	1.000
Myalgia	72	88.9	17	89.	1.000
Arthralgia	73	90.1	17	89.5	1.000
Retro-orbital pain	66	81.5	14	73.7	0.525
Prostration	73	90.1	17	89.5	1.000
Rash	46	56.8	11	57.9	1.000
Neck stiffness	45	55.6	8	42.1	0.423
Sore throat	48	59.3	9	47.4	0.493
Melena	13	16.0	2	10.5	0.729
Spontaneous bleeding	26	32.1	7	36.8	0.901
Gastrointestinal symptoms	6	7.4	2	10.5	0.645
Hepatomegaly	67	82.7	17	89.5	0.730
Splenomegaly	37	45.7	10	52.6	0.771
Breathing difficulty	33	40.7	9	47.4	0.788
Pleural effusion	16	19.8	3	15.8	1.000
Bleeding	21	25.9	7	36.8	0.503

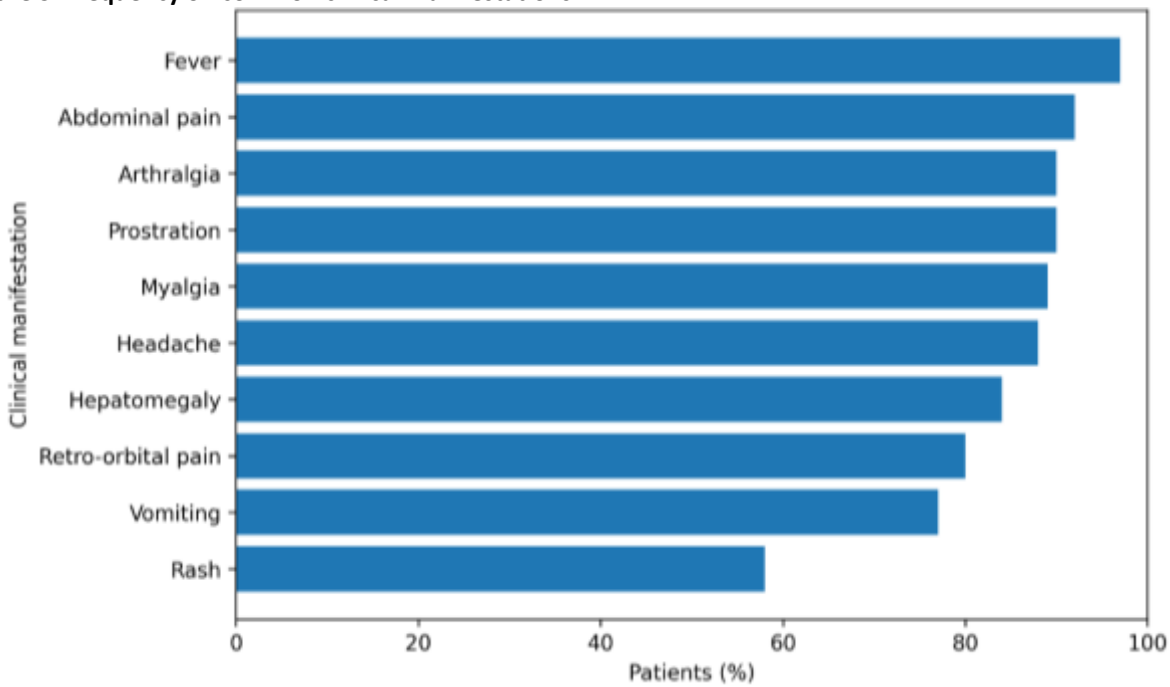
Hematological and biochemical comparison

Median hematological and biochemical parameters were compared between non-severe and severe dengue using the Mann Whitney U test. No parameter demonstrated a statistically significant difference between the two severity groups. The median platelet count was 45,000/µL in non-severe dengue and 40,000/µL in severe dengue (p=0.183), while median AST and ALT were 153 U/L and 151 U/L in non-severe disease versus 233 U/L and 163 U/L in severe disease, respectively. Spearman analysis of the composite clinical-manifestation burden showed a weak inverse correlation with hematocrit (rho=-0.236, p=0.018), whereas correlations with platelet count (rho=-0.123, p=0.224), INR (rho=0.195, p=0.052), AST (rho=0.004, p=0.971), ALT (rho=0.054, p=0.599), albumin (rho=-0.111, p=0.274) and the remaining parameters were not statistically significant. These exploratory correlations should not be interpreted as causal relationships. (Table 3) (Fig 3)

Table 3. Hematological and Biochemical Parameters According to Disease Severity

	Non-severe		Severe		
Parameter	**Median**	**(IQR)**	**Median**	**(IQR)**	**p-value**
Hemoglobin (g/dL)	11.60	10.10–13.40	11.50	10.55–13.20	0.728
TLC (×10³/µL)	5.50	3.80–9.70	4.71	2.91–9.80	0.458
MCV (fL)	91.90	85.40–105.20	86.90	80.60–102.45	0.361
Hematocrit (%)	35.60	30.40–42.20	35.40	33.35–41.60	0.752
Platelet count (/µL)	45,000	22,000–74,000	40,000	16,750–52,500	0.183
INR	1.11	0.94–1.51	1.02	0.90–1.30	0.347
Total bilirubin	0.73	0.50–1.02	0.74	0.50–1.33	0.437
SGOT/AST	153	70–325	233	154–433.50	0.160
SGPT/ALT	151	84–252	163	115.50–389.50	0.210
Total protein	6.60	6.10–7.00	6.30	6.05–7.20	0.772
Albumin	3.60	3.20–4.00	3.50	3.40–3.60	0.281
Serum creatinine	0.97	0.85–1.17	0.90	0.86–1.08	0.532
Serum urea	23.64	15.77–36.25	21.89	13.39–32.91	0.314

Figure 3. Frequency of common clinical manifestations.



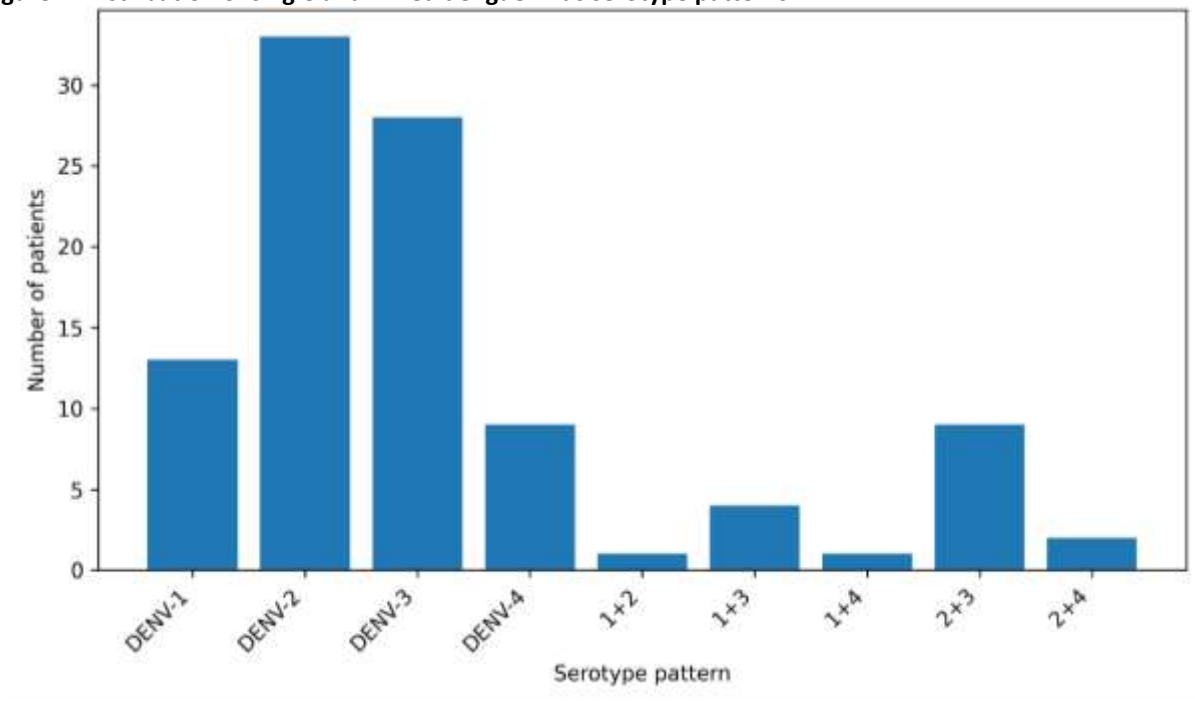
Dengue serotype distribution

All four dengue serotypes were detected. DENV-2 was the most frequent single-serotype pattern (33%), followed by DENV-3 (28%), DENV-1 (13%) and DENV-4 (9%). Mixed-serotype infections accounted for 17% of patients: DENV-2+DENV-3 was the most frequent mixed pattern (9%), followed by DENV-1+DENV-3 (4%), DENV-2+DENV-4 (2%), DENV-1+DENV-2 (1%) and DENV-1+DENV-4 (1%). Mixed-serotype infection was strongly associated with severe dengue. Severe disease occurred in 10/17 (58.8%) patients with mixed infection compared with 9/83 (10.8%) patients with single-serotype infection (Fisher's exact $p<0.001$). The DENV-2+DENV-3 pattern was particularly associated with severity: 6 of 9 patients (66.7%) with this pattern were severe compared with 13 of 91 (14.3%) among all other patterns (Fisher's exact $p=0.0013$). Because several serotype categories contained very small numbers, these associations should be interpreted as exploratory and require confirmation in larger cohorts (Table 4) (Fig 4)

Table 4. Distribution of Dengue Virus Serotype Patterns and Disease Severity

Serotype pattern	n	Percent	Severe n	Severe within pattern (%)
DENV-1	13	13.0%	3	23.1%
DENV-2	33	33.0%	3	9.1%
DENV-3	28	28.0%	3	10.7%
DENV-4	9	9.0%	0	0.0%
DENV-1 + DENV-2	1	1.0%	1	100.0%
DENV-1 + DENV-3	4	4.0%	1	25.0%
DENV-1 + DENV-4	1	1.0%	0	0.0%
DENV-2 + DENV-3	9	9.0%	6	66.7%
DENV-2 + DENV-4	2	2.0%	2	100.0%

Figure 4. Distribution of single and mixed dengue virus serotype patterns.



5. Discussion

This hospital based cross-sectional analysis of 100 dengue patients demonstrates three principal findings. First, the cohort had a broad clinical spectrum, with 19% classified as severe dengue and a high frequency of abdominal pain, arthralgia, prostration, myalgia and hepatomegaly. Second, all four DENV serotypes circulated, with DENV-2 the most common single serotype infection and 17% of patients showing mixed-serotype patterns. Third, mixed serotype infection was strongly associated with severe disease, particularly DENV-2+DENV-3, whereas the routine hematological and biochemical variables did not reach statistical significance in the overall severe vs non-severe comparison.

The predominance of DENV-2 in the present dataset is consistent with recent Indian molecular surveillance, although the magnitude of DENV-2 predominance varies considerably between regions and seasons. A 2026 pan-India molecular surveillance study reported DENV-2 as the predominant serotype and found increased likelihood of thrombocytopenia, arthralgia and hemorrhagic manifestations in concurrent infections (Deshpande et al., 2026). A recent hospital-based study from Karnataka also reported DENV-2 predominance, while not finding a significant association between individual serotypes and severity (Patil et al., 2026). These observations emphasize that local serotype surveillance is necessary rather than assuming a uniform national pattern.

The association between mixed infection and severe disease in this dataset is notable. Ten of 17 patients with mixed serotypes were classified as severe, compared with 9 of 83 patients with single-serotype infection. This finding is directionally consistent with recent surveillance evidence suggesting that concurrent infections can be associated with thrombocytopenia and hemorrhagic manifestations. However, the present sample is small, and mixed infections were represented by several different combinations. Therefore, the observed association should be regarded as hypothesis-generating rather than definitive.

With respect to laboratory markers, the absence of statistically significant differences should be interpreted carefully. Previous systematic reviews and prognostic studies have identified lower platelet counts, higher AST/ALT, hypoalbuminemia and selected changes in hematocrit as useful markers of progression to severe dengue (Sangkaew et al., 2021; Tsheten et al., 2021; Huy & Toàn, 2022). The present analysis was cross-sectional and used values captured in a heterogeneous clinical phase; timing of blood sampling can substantially influence these biomarkers. In addition, all participants had platelet counts below 100,000/µL, restricting the ability to discriminate severity on the basis of thrombocytopenia alone.

The clinical pattern in this cohort is broadly compatible with the established dengue spectrum. Fever, headache, myalgia, arthralgia, vomiting and abdominal pain are common manifestations, while warning signs such as bleeding, fluid accumulation and hepatomegaly are clinically important for severity assessment. The WHO framework emphasizes severe plasma leakage, severe bleeding and severe organ involvement as defining pathways to severe dengue (WHO, 2009). Meta-analytic evidence similarly supports the importance of abdominal pain, vomiting, hepatomegaly, pleural effusion and hematocrit/platelet changes as warning features (Tsheten et al., 2021).

The observed age pattern is also relevant. Severe disease was proportionally more common in older age groups, with the highest proportion in patients >60 years. However, the oldest age groups contained few participants, so the apparent gradient should not be interpreted as a stable population estimate. Larger prospective studies with multivariable adjustment are required to separate age effects from serotype, secondary infection, timing of presentation and other clinical factors.

6. Conclusion

In this cohort of 100 hospitalized dengue patients, all four DENV serotypes were identified, with DENV-2 being the most frequent single serotype and mixed infections occurring in 17% of patients. Severe dengue occurred in 19% of participants. Routine hematological and biochemical parameters showed no statistically significant severe versus non-severe differences in this dataset, although hematocrit showed a weak inverse correlation with overall manifestation burden. In contrast, mixed-serotype infection was strongly associated with severe disease, particularly DENV-2+DENV-3. These findings support the value of molecular serotyping alongside systematic clinical assessment and laboratory monitoring. Larger multicenter prospective studies with standardized sampling times, validated molecular methods and multivariable modelling are warranted.

7. References

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