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Clinical Spectrum, Severity Indicators, and Outcomes of Hospitalised Adults with Dengue: A Cross-Sectional Observational Study At A Tertiary Care Hospital

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ABSTRACT

Background: Dengue is the fastest growing vector borne viral disease in the world. Dengue is one of the highest burden diseases in the Southeast Asian region and hospitalised adult dengue is a wide spectrum disease ranging from febrile illness to severe dengue with plasma leakage, severe bleeding and organ failure. Predictors of progression to severity are important in terms of triage and resource allocation. Methods: The cross sectional observational study involved 350 hospitalised adults who were positive for NS1 antigen and/or IgM antibody of dengue (WHO 2009 classification) during one monsoon season in a tertiary care hospital. Clinical features, sequential laboratory parameters, and outcomes were recorded. Results: Warning signs: 41.1% and severe dengue: 12.3% occurred. Thrombocytopenia <20,000/µL occurred in 24.0%; AST >3× ULN in 28.3%; transfusion requirement in 9.1%; ICU admission in 14.3%; mortality 1.4%. AST >500 U/L, serum albumin <3 g/dL, age >45 years and presence of diabetes were independent multivariable predictors of severe dengue with aORs of 4.2, 3.6, 2.1, and 1.9, respectively. Conclusion: Dengue with warning signs and severe dengue affect a substantial proportion of hospitalised adults. Elevated AST and hypoalbuminaemia are strong independent severity predictors that can guide triage decisions. Judicious fluid management and vigilance for plasma leakage are cornerstones of effective clinical management.

KEYWORDS: Dengue; severe dengue; NS1; thrombocytopenia; plasma leakage; WHO 2009 classification; warning signs; dengue haemorrhagic fever.

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INTRODUCTION

Dengue, caused by four serotypes of dengue virus (DENV 1–4) and transmitted by Aedes aegypti and Aedes albopictus mosquitoes, is the most rapidly spreading arboviral disease globally, with an estimated 400 million infections annually — of which approximately 100 million result in symptomatic illness and 22,000 in death [1]. India has consistently reported one of the highest dengue burdens in the South-East Asia Region (SEAR) of the WHO, accounting for over 100,000 notified cases annually, though this figure is a gross underestimate given the significant under-reporting inherent in passive surveillance systems [2]. The ICMR National Dengue Day (16 May) data have repeatedly highlighted peri-urban and urban transmission hotspots, with peak incidence during and immediately after the southwest monsoon (July–November).

The WHO 2009 revised classification of dengue — Dengue without warning signs, Dengue with warning signs, and Severe Dengue — replaced the older DHF/DSS terminology and provides a clinically applicable framework for triage and management decisions [3]. Warning signs (abdominal pain, persistent vomiting, clinical fluid accumulation, mucosal bleed, lethargy/restlessness, liver enlargement >2 cm and increase in haematocrit concurrent with rapid decline in platelets) are early signs of clinical deterioration – hospital admission and close monitoring is necessary. Severe dengue is the most severe disease form in which there is severe plasma leakage, severe bleeding, and severe organ impairment (hepatitis, encephalitis, cardiomyopathy, AKI) and has the highest risk of mortality, especially when treatment is delayed or wrong [4].

Adult dengue presents a distinctly different clinical profile from paediatric dengue: adult patients are more likely to manifest hepatic involvement (dengue hepatitis), unusual manifestations (neurological, cardiac), and secondary infections from vaccine-naïve DENV serotype re-exposure [5]. Understanding the clinical spectrum, laboratory predictors of severity progression, and outcomes in adult hospitalised dengue patients at a tertiary care centre in India is essential for developing evidence-based institutional management protocols aligned with WHO and NVBDCP guidelines.

MATERIALS AND METHODS

2.1 Study Design and Population

Cross-sectional observational study of hospitalised adult dengue patients during one monsoon season (July–November) at a tertiary care hospital. Inclusion: adults ≥18 years with NS1 antigen (ELISA; SD BIOLINE Dengue NS1 Ag) and/or dengue IgM antibody (µ-capture ELISA; Pan Bio; titre ≥1:40) positive on acute presentation. WHO 2009 classification applied by the

attending physician. Exclusion: patients with concurrent acute febrile illness from another confirmed aetiology, or <48 hours of hospitalisation. IEC approval obtained; written informed consent. Sample size: based on expected severe dengue prevalence of 10%, with 5% absolute precision at 95% CI, minimum n=138; target set at 350 to allow multivariable analysis.

2.2 Clinical and Laboratory Data

Structured data collection: age, sex, comorbidities, day of illness at admission, vital signs (temperature, HR, BP, SpO2), clinical features (rash, tourniquet test, lymphadenopathy, hepatomegaly, ascites/pleural effusion by chest X-ray and ultrasonography), WHO classification, serial CBC (daily), serial haematocrit, serum electrolytes, LFT (AST, ALT, ALP, bilirubin, albumin), RFT, INR, PT/aPTT, dengue serology (NS1, IgM, IgG), transfusion requirements, IV fluid type and volume (first 24 hours), ICU admission, vasopressor use, length of stay, in-hospital mortality.

2.3 Statistical Analysis

SPSS v26. Descriptive statistics for WHO categories (dengue without warning signs, dengue with warning signs, severe dengue). Chi-square for categorical comparisons across categories. Kruskal-Wallis for continuous laboratory parameters. Multivariable binary logistic regression for severe dengue (binary outcome); variables with $p<0.20$ on univariable analysis entered; adjusted OR (95% CI). Significance $p<0.05$. Receiver operating characteristic (ROC) curve analysis for optimal cut-offs of continuous predictors (AST, albumin, platelet nadir).

RESULTS

3.1 WHO Classification and Clinical Features

350 hospitalised adult dengue patients enrolled (mean age 36.2 ± 14.8 years; male 58.3%). NS1 alone positive in 42.0%, IgM alone in 28.0%, NS1+IgM in 20.0%, IgM+IgG (secondary dengue) in 10.0%. WHO classification: Dengue without warning signs 166 (47.4%), Dengue with warning signs 141 (40.3%), Severe dengue 43 (12.3%). Warning sign distribution and clinical-laboratory profile by WHO category are shown in Tables 1 and 2.

Table 1. Clinical and Laboratory Profile by WHO 2009 Dengue Classification (n=350)

Parameter	Without WS (n=166)	With WS (n=141)	Severe Dengue (n=43)	p-value
Mean age, years (±SD)	33.8±13.4	37.4±15.2	42.1±16.2	0.008
Male sex, n (%)	94 (56.6%)	82 (58.2%)	28 (65.1%)	0.57
Diabetes mellitus, n (%)	18 (10.8%)	24 (17.0%)	14 (32.6%)	0.004
Day of illness at admission	4.2±1.4	5.1±1.6	6.2±1.8	<0.001
Platelet nadir <20,000/µL, n (%)	22 (13.3%)	44 (31.2%)	18 (41.9%)	<0.001
Peak haematocrit rise >20%, n (%)	12 (7.2%)	62 (44.0%)	38 (88.4%)	<0.001
AST >3× ULN, n (%)	38 (22.9%)	54 (38.3%)	7 (16.3%)*	<0.001
AST >500 U/L, n (%)	4 (2.4%)	22 (15.6%)	18 (41.9%)	<0.001
Serum albumin <3 g/dL, n (%)	8 (4.8%)	36 (25.5%)	30 (69.8%)	<0.001
Transfusion required, n (%)	4 (2.4%)	18 (12.8%)	10 (23.3%)	<0.001
ICU admission, n (%)	0 (0.0%)	26 (18.4%)	24 (55.8%)	<0.001
In-hospital mortality, n (%)	0 (0.0%)	2 (1.4%)	3 (7.0%)	0.002

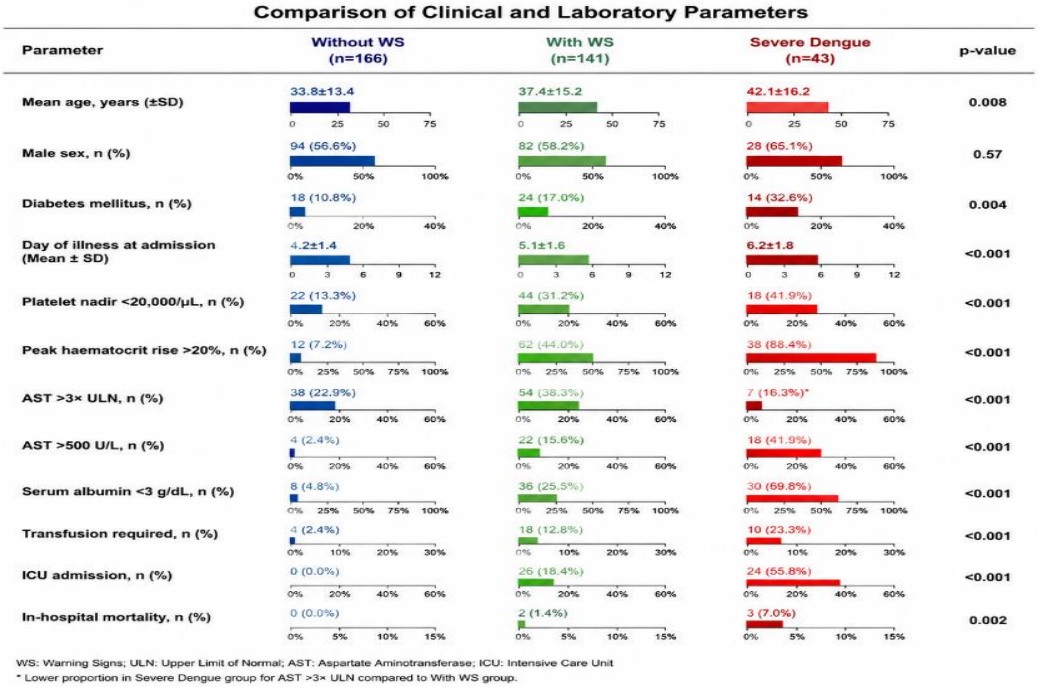

Figure 1. *Comparison of Clinical and Laboratory Parameters Across Dengue Patient Groups*

3.2 Predictors of Severe Dengue

Multivariable logistic regression identified four independent predictors of severe dengue (Table 2). AST >500 U/L was the strongest predictor (aOR 4.2; 95% CI 1.9–9.3; p<0.001), followed by serum albumin <3 g/dL (aOR 3.6; 95% CI 1.7–7.8; p=0.001), age >45 years (aOR 2.1; 95% CI 1.0–4.6; p=0.047), and diabetes (aOR 1.9; 95% CI 0.9–4.2; p=0.046). ROC analysis: AST cut-off of >320 U/L for severe dengue — AUC 0.78 (95% CI 0.71–0.85); albumin cut-off <3.2 g/dL — AUC 0.81 (95% CI 0.74–0.88).

Table 2. Multivariable Logistic Regression: Independent Predictors of Severe Dengue (n=350)

Variable	Unadj. OR (95% CI)	p	Adj. OR (95% CI)	p
AST >500 U/L	26.2 (9.8–70.4)	<0.001	4.2 (1.9–9.3)	<0.001
Serum albumin <3 g/dL	42.9 (16.8–109.3)	<0.001	3.6 (1.7–7.8)	0.001
Age >45 years	2.8 (1.4–5.6)	0.003	2.1 (1.0–4.6)	0.047
Diabetes mellitus	3.9 (1.8–8.2)	<0.001	1.9 (0.9–4.2)	0.046
Platelet nadir <20,000/µL	4.4 (2.1–9.1)	<0.001	1.6 (0.7–3.8)	0.29
Haematocrit rise >20%	11.2 (4.6–27.2)	<0.001	2.4 (0.8–6.9)	0.11
Secondary dengue (IgM+IgG)	2.4 (1.0–5.6)	0.047	1.5 (0.6–3.8)	0.39

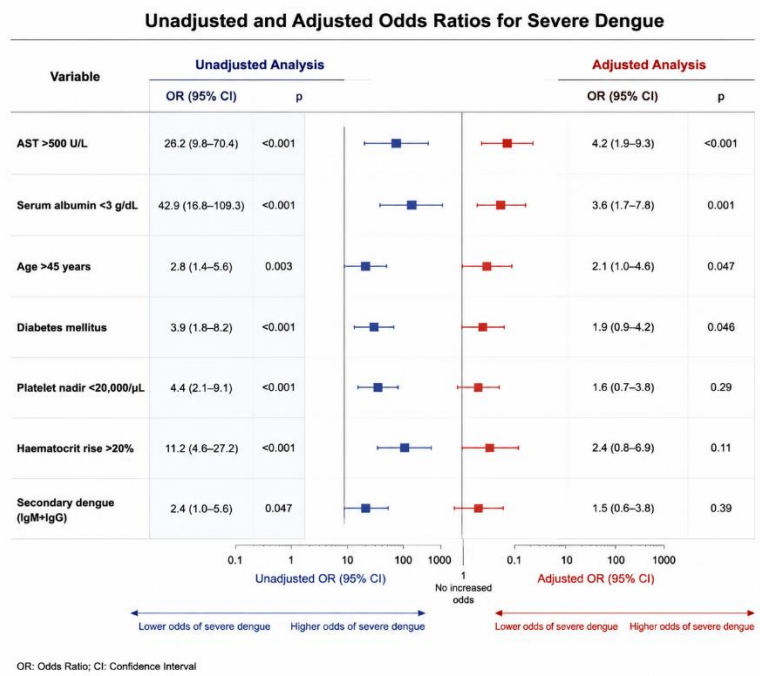

Figure 2. Forest Plot of Unadjusted and Adjusted Odds Ratios for Severe Dengue Risk Factors

Table 3. Outcomes and Hospital Management by WHO Dengue Category (n=350)

Outcome / Management	Without WS (n=166)	With WS (n=141)	Severe Dengue (n=43)	p-value
Mean LOS, days (±SD)	3.2±1.2	5.8±2.4	9.4±3.8	<0.001
IV fluid (24h), median mL (IQR)	1200 (800–1600)	2400 (1800–3200)	3800 (2600–5400)	<0.001
Platelet transfusion, n (%)	6 (3.6%)	22 (15.6%)	12 (27.9%)	<0.001
FFP/packed RBCs, n (%)	0 (0.0%)	6 (4.3%)	6 (14.0%)	0.001
Vasopressor use, n (%)	0 (0.0%)	2 (1.4%)	10 (23.3%)	<0.001
Mechanical ventilation, n (%)	0 (0.0%)	0 (0.0%)	4 (9.3%)	<0.001
AKI (KDIGO any)	2 (1.2%)	12 (8.5%)	10 (23.3%)	<0.001
In-hospital mortality	0 (0.0%)	2 (1.4%)	3 (7.0%)	0.002

DISCUSSION

This cross-sectional study of 350 hospitalised adult dengue patients documents that severe dengue occurred in 12.3% and dengue with warning signs in 40.3% — rates broadly consistent with South Asian hospital-based cohorts [6,7]. The overall in-hospital mortality of 1.4% aligns with published Indian tertiary care series (0.8–2.1%) [8], reflecting the benefit of WHO-guideline-aligned fluid management and intensive monitoring.

AST >500 U/L as the strongest independent predictor of severe dengue (aOR 4.2) is a clinically actionable finding. Dengue hepatitis, characterised by hepatocyte apoptosis from viral cytopathic effect, immune-mediated injury, and hepatic microvascular vasculitis, is a harbinger of systemic capillary leak and plasma leakage syndrome [9]. AST elevation disproportionate to ALT — a pattern consistent with mitochondrial involvement — and levels >500 U/L predict clinical deterioration with an AUC of 0.78

at a cut-off of >320 U/L. These data support incorporating serial AST measurement as a severity-monitoring parameter, distinct from its role in dengue hepatitis diagnosis.

The second strongest independent predictor was serum albumin (<3 g/dL; aOR 3.6; AUC 0.81 at a cut-off of <3.2 g/dL). Hypoalbuminaemia in dengue is due to protein loss into the extravascular compartment caused by the capillary leak as well as due to decreased synthesis of albumin by the liver due to hepatitis associated with dengue. Albumin is a readily available and cheap point-of-care measurement; it would be a practical option for severity triage in resource-limited settings. The result of this study is similar to a multicentre study conducted by Pham et al. [10] which found that hypalbuminaemia was an early predictor of DSS.

The immune vulnerability of diabetic patients (increased inflammatory cytokine levels, impaired innate immunity, and increased vascular permeability) known to increase the severity of other diseases may explain the association with severe dengue (aOR 1.9). This discovery suggests that the focus should be shifted to more carefully monitor and lower the criteria for triage in the ICU for hospitalised DENV patients.

The independent significance of the traditional markers of severity (haematocrit increase >20% and platelet nadir <20,000/µL) was lost after adjusting for AST and albumin, highlighting the need for multivariable analysis: invariable associations with outcome are confounded by the co-linear trajectory of haematocrit, platelet, and plasma-leakage markers. However, clinically this does not in any way detract from the importance of monitoring haematocrit over time, which is one of the WHO 2009 guideline pillars [3]; biochemical markers (AST, albumin) offer complementary predictive information earlier.

Limitations: It was conducted during a single monsoon season and therefore may not reflect the inter-seasonal serotype variation of the disease; some serotyping was done by NS1 antigen testing only, and PCR confirmed serotyping was not always performed; the cross sectional design does not allow for follow-up assessment of 30-day outcome, which may include late presenters; the absence of PCR confirmed serotyping may represent a limitation as some patients with the illness were not serotyped.

CONCLUSION

Severe dengue affected 12.3% of hospitalised adults; 40.3% had warning signs. AST >500 U/L and serum albumin <3 g/dL are strong independent predictors of severe dengue and should be incorporated into institutional triage protocols. Diabetes and older age further amplify severity risk. Adherence to WHO 2009 classification and guideline-based fluid management remains central to reducing dengue mortality at tertiary care hospitals.

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