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Original Research Article

Clinical Profile of Dengue Fever and Its Association with Disease Severity: A Longitudinal Study from a Tertiary Care Teaching Hospital in Southern India

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Abstract

Background: Dengue produces a clinical spectrum ranging from an undifferentiated febrile illness to severe plasma leakage, haemorrhage and organ failure. Because specific antiviral therapy is unavailable, outcome depends almost entirely on early recognition of patients who are progressing towards severe disease. Bedside clinical features and routinely available serological and radiological findings therefore retain considerable triage value in resource-limited settings.

Objectives: To describe the clinical profile of serologically confirmed adult dengue patients and to determine which clinical, serological and radiological features are associated with disease severity as defined by the World Health Organization (WHO) 2009 classification.

Methods: A longitudinal, hospital-based study was conducted in the Department of General Medicine, McGann District Teaching Hospital, Shivamogga, Karnataka, between January 2021 and June 2022. All consecutive adults (>18 years) positive for dengue NS1 antigen or IgM by enzyme-linked immunosorbent assay (ELISA) were enrolled after written informed consent; patients with pre-existing hepatic disease, alcoholic hepatitis, hepatotoxic drug exposure or co-infections causing transaminase elevation were excluded. Participants were classified as dengue without warning signs, dengue with warning signs or severe dengue. Categorical variables were compared using the chi-square or Fisher's exact test and continuous variables using one-way analysis of variance (ANOVA), with $p<0.05$ considered significant.

Results: Of 130 patients, 75 (57.7%) were male and the mean age was 40.41 ± 15.95 years. Seventy-five (57.7%) had dengue without warning signs, 40 (30.8%) had dengue with warning signs and 15 (11.5%) had severe dengue. Fever was universal (100%), followed by headache (82.3%), myalgia (80.0%), arthralgia (68.5%), vomiting (45.4%), haemorrhagic manifestations (21.5%), rash (17.7%) and abdominal pain (14.6%). Longer duration of fever at presentation ($p=0.003$), headache ($p=0.049$), abdominal pain ($p=0.037$) and haemorrhagic manifestations ($p=0.016$) were significantly associated with severity. NS1 antigen positivity was highest in severe dengue (80.0%) and IgM positivity highest in dengue without warning signs (78.7%) ($p=0.041$ and $p=0.022$, respectively).

Conclusion: Abdominal pain, haemorrhagic manifestations, prolonged fever, NS1 antigen positivity and abnormal chest and abdominal imaging identify adults at risk of severe dengue. These are inexpensive, widely available bedside markers and should prompt intensified monitoring in district hospital settings.

Keywords: Dengue; Severe Dengue; Clinical Profile; NS1 Antigen; Warning Signs; India.
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Introduction

Dengue is the most rapidly expanding arboviral infection in the world. It is caused by four antigenically distinct serotypes (DENV-1 to DENV-4) of a single-stranded RNA virus of the family Flaviviridae, transmitted principally by Aedes aegypti and, to a lesser extent, by Aedes albopictus.[1,2] Modelling studies estimate that approximately 390 million infections occur globally each year, of which about 96 million are clinically apparent, and that nearly half the world's population now lives in areas where transmission is possible.[3] Cases reported to the World Health

Organization (WHO) increased more than eightfold between 2000 and 2019, and dengue is now endemic in more than 100 countries, with the greatest burden falling on the Regions of the Americas, South-East Asia and the Western Pacific.[4]

India carries a disproportionate share of this burden. A nationally representative serosurvey demonstrated that roughly half of the Indian population aged 5–45 years had serological evidence of past dengue infection, with wide inter-state variation.[5] A systematic review and meta-analysis of Indian studies confirmed year-round transmission with monsoon-related peaks and documented the spread of dengue from urban centres into peri-urban and rural districts, including much of Karnataka.[6] Consequently, district-level hospitals — rather than tertiary referral centres — now manage the majority of dengue admissions, often without access to virological typing, serial haematocrit monitoring or intensive care.

Clinically, dengue is a dynamic illness with three recognised phases: a febrile phase, a critical phase during which increased vascular permeability may lead to plasma leakage, and a recovery phase.[7] Most infections are self-limiting, but a minority progress to severe dengue characterised by severe plasma leakage with shock, severe bleeding or severe organ impairment.[1] Because deterioration typically occurs around defervescence — precisely when the patient may appear to be improving — the WHO revised its classification in 2009 to a three-tier scheme of dengue without warning signs, dengue with warning signs and severe dengue.[1] The warning signs (abdominal pain, persistent vomiting, mucosal bleeding, lethargy, clinical fluid accumulation, hepatomegaly and a rising haematocrit with falling platelet count) were intended to be simple enough for use at the point of first contact.[8]

In practice, however, the early clinical features of dengue overlap substantially with those of malaria, enteric fever, leptospirosis, scrub typhus and other undifferentiated febrile illnesses endemic to the same regions.[9] Confirmatory virological tests such as reverse transcription polymerase chain reaction are rarely available outside reference laboratories, and even NS1 antigen and IgM ELISA assays vary in sensitivity depending on the day of illness and the immune status of the host.[10,11] Radiological evidence of plasma leakage — pleural effusion on chest radiography, and ascites, gallbladder wall oedema or polyserositis on abdominal ultrasonography — has been shown to precede haemodynamic decompensation and may therefore serve as an accessible surrogate marker of the critical phase.[12,13]

Against this background, a clear description of which bedside features actually discriminate between severity grades in adult Indian patients remains clinically valuable. Most published Indian series are cross-sectional, paediatric, or predate the 2009 classification. The present study was therefore undertaken to characterise the clinical profile of adults admitted with serologically confirmed dengue at a district teaching hospital in Shivamogga, Karnataka, and to identify the clinical, serological and radiological features associated with disease severity.

Materials and Methods

This was a longitudinal, hospital-based observational study conducted in the Department of General Medicine, McGann District Teaching Hospital, Shivamogga, Karnataka, a public teaching hospital serving a largely semi-urban and rural catchment population in the Malnad region of southern India. The study period extended from January 2021 to June 2022 (18 months).

Study Population and Sampling: All consecutive patients admitted to the Department of General Medicine during the study period with serologically confirmed dengue were considered for enrolment. As this was a time-bound study, no a priori sample size was calculated; every eligible patient presenting during the 18-month window was included, yielding a final sample of 130 participants.

Inclusion Criteria: Men and women aged more than 18 years who tested positive for dengue-specific IgM antibody by ELISA and/or for dengue non-structural protein 1 (NS1) antigen by ELISA.

Exclusion Criteria: Patients with a documented history of hepatic dysfunction; patients with alcoholic hepatitis (defined by an aspartate aminotransferase to alanine aminotransferase ratio ≥2:1); patients with any co-infection independently capable of raising hepatic transaminases; and patients with a history of known hepatotoxic drug use within the preceding six months. These criteria were applied to ensure that observed biochemical derangements could reasonably be attributed to dengue.

Data Collection: Written informed consent was obtained from each participant in their own language after the purpose of the study had been explained. Data were collected using a pre-tested, semi-structured proforma covering sociodemographic details, presenting complaints, duration of fever prior to admission, past and personal history, and a complete physical examination. A structured symptom checklist was completed for every patient and comprised fever, headache, myalgia, arthralgia, retro-orbital pain, rash, vomiting, abdominal pain and any haemorrhagic manifestation. Bleeding was further

categorised as petechiae, ecchymosis, purpura, gum bleeding, haematuria, malaena or haematemesis. A detailed systemic examination — vital signs, general physical examination and examination of the respiratory, cardiovascular, gastrointestinal and central nervous systems — was performed on admission and repeated daily until discharge.

Investigations: All participants underwent a complete haemogram, liver function tests, renal function tests, prothrombin time with international normalised ratio and activated partial thromboplastin time, chest radiography (postero-anterior view) and ultrasonography of the abdomen. Chest radiographs were reported as abnormal in the presence of pleural effusion or other evidence of fluid accumulation; abdominal ultrasonograms were reported as abnormal in the presence of ascites, gallbladder wall thickening, hepatomegaly or polyserositis. Additional investigations were performed as clinically indicated.

Classification of Severity: Patients were assigned to one of three mutually exclusive categories according to the WHO 2009 classification: dengue without warning signs, dengue with warning signs, and severe dengue (severe plasma leakage, severe bleeding or severe organ involvement).[1]

Statistical Analysis: Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version 24.0 (IBM Corp., Armonk, NY, USA). Qualitative data were expressed as frequencies and proportions and quantitative data as mean ± standard deviation. Associations between categorical variables were tested using the chi-square test or Fisher's exact test as appropriate, and differences in means across the three severity groups were tested using one-way analysis of variance. A p-value <0.05 was considered statistically significant and a p-value <0.001 highly significant.

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee, and the study was conducted in accordance with the Declaration of Helsinki. Participation was voluntary and confidentiality was maintained throughout.

Results

A total of 130 serologically confirmed adult dengue patients were enrolled over 18 months.

Table 1: Distribution of study participants by severity of dengue (n=130)

Severity category (WHO 2009)	Number of patients	Percentage
Dengue without warning signs	75	57.7%
Dengue with warning signs	40	30.8%
Severe dengue	15	11.5%
Total	**130**	**100.0%**

More than half the cohort presented without warning signs, while approximately one in nine patients met criteria for severe dengue. Among the 15 patients with severe dengue, severe bleeding was the commonest defining manifestation (8 patients, 53.3%), followed by severe plasma leakage (4 patients, 26.7%) and severe organ involvement (3 patients, 20.0%).

Table 2: Age distribution across severity groups

Age group (years)	Severe dengue n (%)	Dengue with warning signs n (%)	Dengue without warning signs n (%)	Total n (%)
17–26	1 (6.67)	10 (25.00)	23 (30.67)	34 (26.15)
27–36	5 (33.33)	5 (12.50)	12 (16.00)	22 (16.92)
37–46	5 (33.33)	7 (17.50)	15 (20.00)	27 (20.77)
47–56	2 (13.33)	11 (27.50)	11 (14.67)	24 (18.46)
57–66	0 (0.00)	6 (15.00)	12 (16.00)	18 (13.85)
67–76	1 (6.67)	0 (0.00)	1 (1.33)	2 (1.54)
77–86	1 (6.67)	1 (2.50)	1 (1.33)	3 (2.31)
Total	**15 (100)**	**40 (100)**	**75 (100)**	**130 (100)**
Mean age ± SD	**41.53 ± 15.38**	**41.80 ± 16.03**	**39.44 ± 16.17**	**40.41 ± 15.95** (p=0.724)

Dengue affected predominantly young and middle-aged adults, with 63.8% of the cohort aged below 47 years. Mean age did not differ significantly across the three severity strata (p=0.724), indicating that within this adult population age was not a determinant of severity.

Table 3: Sex distribution across severity groups

Sex	Severe dengue n (%)	Dengue with warning signs n (%)	Dengue without warning signs n (%)	Total n (%)	p-value
Male	10 (66.7)	26 (65.0)	39 (52.0)	75 (57.7)	0.306
Female	5 (33.3)	14 (35.0)	36 (48.0)	55 (42.3)	

Males outnumbered females with a male-to-female ratio of 1.36:1. Although the proportion of males rose progressively with severity (52.0% → 65.0% → 66.7%), this trend did not reach statistical significance (p=0.306).

Table 4: Duration of fever at presentation

Duration of fever	Severe dengue n (%)	Dengue with warning signs n (%)	Dengue without warning signs n (%)	Total n (%)	p-value
1–2 days	0 (0.0)	6 (15.0)	14 (18.7)	20 (15.4)	0.003
2–3 days	0 (0.0)	4 (10.0)	10 (13.3)	14 (10.8)	
3–4 days	4 (26.7)	17 (42.5)	27 (36.0)	48 (36.9)	
4–5 days	2 (13.3)	6 (15.0)	15 (20.0)	23 (17.7)	
5–6 days	3 (20.0)	5 (12.5)	5 (6.7)	13 (10.0)	
6–7 days	6 (40.0)	2 (5.0)	4 (5.3)	12 (9.2)	

Duration of fever showed a highly significant association with severity (p=0.003). No patient with severe dengue presented within the first three days of fever, whereas 40.0% of the severe dengue group presented after six or more days of fever, compared with only 5.0% and 5.3% in the warning-sign and no-warning-sign groups respectively. This pattern is consistent with severe manifestations emerging at or after defervescence, during the critical phase.

Table 5: Clinical manifestations and their association with dengue severity

Clinical feature (present)	Severe dengue (n=15)	Dengue with warning signs (n=40)	Dengue without warning signs (n=75)	Total (n=130)	p-value
Fever	15 (100.0%)	40 (100.0%)	75 (100.0%)	130 (100.0%)	—
Headache	13 (86.7%)	28 (70.0%)	66 (88.0%)	107 (82.3%)	0.049
Myalgia	14 (93.3%)	34 (85.0%)	56 (74.7%)	104 (80.0%)	0.163
Arthralgia	12 (80.0%)	29 (72.5%)	48 (64.0%)	89 (68.5%)	0.383
Vomiting	10 (66.7%)	14 (35.0%)	35 (46.7%)	59 (45.4%)	0.104
Rash	5 (33.3%)	6 (15.0%)	12 (16.0%)	23 (17.7%)	0.467
Abdominal pain	7 (46.7%)	12 (30.0%)	0 (0.0%)	19 (14.6%)	0.037
Haemorrhagic manifestations	12 (80.0%)	16 (40.0%)	0 (0.0%)	28 (21.5%)	0.016

Fever was present in every patient and was therefore not discriminatory.

Headache, myalgia and arthralgia were common across all groups and reflect the classical "break-bone" symptom complex, but only headache reached statistical significance (p=0.049), and the pattern was non-monotonic (lowest in the warning-sign group), so this finding should be interpreted with caution. The two features that discriminated most clearly between severity strata were abdominal pain and haemorrhagic manifestations. Abdominal pain was reported by 46.7% of patients with severe dengue and 30.0% of those with warning signs, but was entirely absent in patients without warning signs (p=0.037). Similarly, haemorrhagic manifestations occurred in 80.0% of severe dengue and 40.0% of warning-sign cases, and in none of the patients without warning signs (p=0.016).

Both are themselves components of the WHO warning-sign definition, and their strong gradient across strata confirms internal consistency of the classification while underscoring their practical value as red-flag symptoms.

Table 6: Types of haemorrhagic manifestations observed

Type of bleeding	Number of episodes	Percentage
Petechiae	8	30%
Gum bleeding	7	26%
Ecchymosis	4	15%
Purpura	3	11%

Haematuria	2	7%
Haematemesis	2	7%
Malaena	1	4%
Total	**27**	**100%**

Cutaneous and mucosal bleeding predominated: petechiae, gum bleeding, ecchymosis and purpura together accounted for 82% of all bleeding episodes. Overt gastrointestinal or genitourinary bleeding (haematemesis, malaena, haematuria) was uncommon (18%) but clinically significant, as these episodes clustered within the severe dengue group.

Table 7: Serological markers and dengue severity

Marker	Severe dengue (n=15)	Dengue with warning signs (n=40)	Dengue without warning signs (n=75)	Total (n=130)	p-value
NS1 antigen positive	12 (80.0%)	17 (42.5%)	36 (48.0%)	65 (50.0%)	0.041
IgM antibody positive	7 (46.7%)	25 (62.5%)	59 (78.7%)	91 (70.0%)	0.022

NS1 antigen positivity was significantly more frequent in severe dengue (80.0%) than in the other two groups (p=0.041), whereas IgM positivity showed the reciprocal pattern, being commonest in dengue without warning signs (78.7%) and least frequent in severe dengue (46.7%) (p=0.022). Rather than implying that NS1 causes severity, this reciprocal relationship most plausibly reflects the timing and immunological context of presentation: NS1 is detectable during early viraemia, while IgM appears from around day five, so a high NS1-to-IgM ratio in the severe group is consistent with high circulating viral antigen load at the time of sampling.

Table 8: Radiological findings and dengue severity

Investigation	Severe dengue (n=15)	Dengue with warning signs (n=40)	Dengue without warning signs (n=75)	Total (n=130)	p-value
Chest radiograph abnormal	8 (53.3%)	6 (15.0%)	0 (0.0%)	14 (10.8%)	0.043
Ultrasonography of abdomen abnormal	10 (66.7%)	8 (20.0%)	0 (0.0%)	18 (13.8%)	0.031

Radiological abnormalities showed a clear severity gradient. Abnormal chest radiographs (predominantly pleural effusion) were seen in 53.3% of severe dengue and 15.0% of warning-sign cases, and abnormal abdominal ultrasonograms (ascites, gallbladder wall oedema, polyserositis) in 66.7% and 20.0% respectively. Neither abnormality was detected in any patient without warning signs (p=0.043 and p=0.031). Imaging evidence of third-space fluid accumulation therefore tracked closely with clinical severity and identified a subgroup of warning-sign patients with subclinical plasma leakage who may warrant closer observation.

Discussion

This longitudinal study of 130 serologically confirmed adult dengue admissions at a district teaching hospital in southern India found a male preponderance (57.7%), a mean age of 40.41 years, and a severity distribution in which 11.5% met WHO criteria for severe dengue. The male excess is consistent with most Indian and South Asian hospital series, including those of Kashinkunti et al.[14] and Patel and Patel,[15] and is generally attributed to greater occupational and outdoor exposure to daytime-biting Aedes vectors as well as differential health-seeking behaviour, rather than to any established biological difference in susceptibility. Notably, sex was not associated with severity in our cohort (p=0.306), a finding echoed by Ahmed et al.[16] although some authors have reported a higher risk of severe disease in females, possibly reflecting a more vigorous cytokine response.[17]

The predominance of young and middle-aged adults, with a non-significant difference in mean age across severity strata (p=0.724), mirrors observations from Deshwal et al.[18] and from Sri Lanka.[19] In hyperendemic settings the adult population remains susceptible to heterotypic serotypes, and secondary infection — rather than chronological age itself — is the principal driver of severe disease.[20]

The symptom profile was dominated by fever (100%), headache (82.3%), myalgia (80.0%) and arthralgia (68.5%), closely matching the distributions reported by Jayadas et al. from Jaffna, Sri Lanka (fever 100%, headache 80.7%, myalgia 50%)[19] and by Kashinkunti et al. from Karnataka.[14] These classical features, however, were poor discriminators of severity, which is unsurprising given that they arise from the systemic inflammatory response common to all symptomatic

dengue.[20] The features that did discriminate — abdominal pain (p=0.037) and haemorrhagic manifestations (p=0.016) — are precisely those incorporated into the WHO warning-sign definition, and their absolute absence in the group without warning signs is a tautological consequence of that classification. Their value therefore lies less in statistical association than in reaffirming that these two symptoms should trigger admission and intensified monitoring at first contact. Petechiae and gum bleeding were the commonest bleeding manifestations, matching the pattern described by Kashinkunti et al.[14] and reflecting the combined contribution of thrombocytopenia, platelet dysfunction and endothelial injury.[21]

Our serological findings warrant careful interpretation. The higher NS1 positivity in severe dengue (80.0%) alongside lower IgM positivity (46.7%) is best explained by sampling during the early viraemic phase, when NS1 concentrations are highest and IgM has not yet appeared; NS1 antigenaemia has been correlated with viral load and with subsequent severity in several cohorts.[10,22] Because our patients with severe dengue also presented later in their fever course, however, the direction of this relationship cannot be established from these data.

The most clinically actionable finding was the radiological gradient. Abnormal chest radiographs and abdominal ultrasonograms were confined to the severe and warning-sign groups (p=0.043 and p=0.031). Serial ultrasonography has previously been shown to detect plasma leakage before haemodynamic compromise becomes clinically apparent,[12,13] and our data support its use as an inexpensive bedside adjunct in district hospitals where serial haematocrit monitoring may be logistically difficult.

The study has limitations. It was conducted at a single centre with a modest sample, and only 15 patients had severe dengue, which limits statistical power and renders subgroup estimates imprecise. Serotyping was not performed, so the contribution of primary versus secondary infection could not be assessed. Finally, patients presenting later in the illness were over-represented among severe cases, introducing potential referral and length-of-illness bias.

Conclusion

In this cohort of 130 adults hospitalised with serologically confirmed dengue, fever, headache, myalgia and arthralgia were near-universal but did not distinguish between severity grades. Disease severity was significantly associated with a longer duration of fever at presentation, abdominal pain, haemorrhagic manifestations, NS1 antigen positivity, and abnormal chest radiographic and abdominal ultrasonographic findings. Petechiae and gum bleeding were the commonest bleeding manifestations, and severe bleeding was the commonest defining feature of severe dengue.

Because all of these markers are obtainable at the bedside or with basic imaging, they are well suited to district-level practice. Adults presenting after the fourth day of fever with abdominal pain or any bleeding manifestation should be regarded as high risk, and a chest radiograph together with an abdominal ultrasonogram should be obtained early to look for evidence of plasma leakage. Prospective multicentre studies with serotyping and serial imaging are required to confirm these associations and to define their predictive performance.

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