



ORIGINAL ARTICLE

## Clinical spectrum of Dengue fever among children: A hospital-based study.

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**ABSTRACT... Objective:** To determine the spectrum of clinical features of dengue fever among patients admitted to a tertiary care hospital in Karachi, Pakistan. **Study Design:** Cross-sectional study. **Setting:** Department of Pediatrics, Zia Uddin Hospital, Karachi, Pakistan. **Period:** September 2023 to February 2024. **Methods:** A total of 84 patients aged 1 month up to 15 years and presenting with dengue fever were analyzed. Demographic data was noted at the time of enrollment, and relevant laboratory investigations were sought. Dengue fever classification, associated clinical features, and final outcomes were noted. Data were analyzed using IBM-SPSS Statistics, version 26.0. **Results:** Of 84 children, 48 (57.1%) were male. The mean age was  $4.58 \pm 3.48$  years. Dengue fever without warning signs, dengue fever with warning signs, and severe dengue fever were diagnosed in 31 (36.9%), 30 (35.7%), and 23 (27.4%) patients, respectively. The frequent presentations were nausea and vomiting (55%), rash (51%), headache (43%), fits (24%), altered mental status (21%), bleeding (21%), and myalgia (17%). Sinus bradycardia on ECG ( $p=0.007$ ), abnormal chest x-ray ( $p=0.005$ ), Ventilatory support ( $p<0.001$ ), and classification of Severe dengue fever ( $< 0.001$ ) were found to be significant predictors of mortality. **Conclusion:** The study identified key clinical features of dengue fever in children, with common symptoms including nausea, rash, headache, and bleeding. Severe dengue, marked by sinus bradycardia, abnormal chest X-ray, and need for ventilatory support, were significantly linked to higher mortality.

**Key words:** Dengue Fever, Headache, Nausea, Rash, Vomiting.

### INTRODUCTION

It is estimated that between 50-100 million new dengue infections occur annually in endemic areas.<sup>1,2</sup> The incubation period of dengue ranges between 3 to 15 days but usually spans between 7 to 10 days.<sup>3</sup> The natural course of dengue infection generally flows from the febrile phase and may follow the critical and relatively long convalescence phase.<sup>4</sup> In the last couple of decades, the burden of dengue has surged, and more than 100 countries have declared endemic globally.<sup>5,6</sup> In Pakistan, the exact prevalence of dengue is not fully known, but 2022 data from World Health Organization (WHO) revealed 25,932 confirmed dengue cases in Pakistan from January to September 2022.<sup>7</sup>

Dengue infection can be asymptomatic (no symptoms), mild, or severe. Common clinical features of dengue may have included fever,

headache, muscle and joint pain, rash, and mild bleeding manifestations.<sup>8</sup> Severe forms of dengue may exhibit hemorrhage/bleeding, organ impairments, and/or plasma leakage, which may lead to shock and fatal outcomes.<sup>9</sup> Compared to adults, pediatric age groups exhibit variety in diagnosing dengue infection.<sup>10,11</sup> Regional data has shown that dengue infection may accompany severe forms that may exhibit gastrointestinal and atypical neurological symptoms.<sup>10</sup>

Studies shedding light on the spectrum and outcomes of dengue among are scarce.<sup>12</sup> This may be because of overlapping signs and symptoms of COVID-19, malaria, and dengue.<sup>13</sup> Missed diagnoses owing to overlapping symptoms and overburdening of the healthcare system are some of the major challenges to the timely diagnosis and management of dengue, especially in a country like Pakistan.

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Given that dengue's manifestations and severity can vary based on factors like virus serotype, immune response, and regional healthcare conditions, understanding these variations is crucial. Accurate identification and timely management of clinical and laboratory factors can help reduce morbidity and mortality. Characterizing both typical and atypical features, especially during outbreaks, is essential for effective diagnosis and treatment. This research was planned to determine the spectrum of different clinical features of dengue fever among patients admitted to a tertiary care private hospital in Karachi, Pakistan.

## METHODS

This descriptive, cross-sectional study was conducted at the Department of Pediatrics, Zia Uddin Hospital, Karachi, Pakistan, from September 2023 to February 2024. A sample size of 84 was calculated taking the proportion of bleeding in dengue fever as 5.8%<sup>10</sup>, with 95% confidence level, and 5% margin of error. The estimated sample size came out to be 84. Non-probability consecutive sampling technique was adopted. Inclusion criteria were children aged above 1 month up to 15 years, and having confirmed dengue. Exclusion criteria were children with concurrent illnesses (enteric fever, malaria, platelet functional defects, etc.) or underlying chronic illnesses. Children on medicines that either affect function or count of platelets were also excluded. Children with preexisting bleeding disorders were also excluded.

Informed and written consents were obtained from parents/guardians of all children enrolled. The study was conducted after getting approval from the ethical review committee of Ziauddin University (letter number: 7100523HRPED, dated: July 15<sup>th</sup> 2023). At enrollment, demographic data like gender and age were noted. Vital signs, relevant laboratory investigations, classification of dengue, and associated clinical features were noted. Dengue was confirmed based on clinical characteristics, low platelet count, and/or positive dengue NS1 or dengue serology positive. Dengue fever was classified as high fever, severe headache, retro-orbital pain, muscle and joint

pain, nausea, vomiting, rash, fatigue, and mild bleeding manifestations such as nosebleeds or gum bleeding in the study population. Dengue with warning signs included patients presenting with persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy or restlessness, liver enlargement greater than 2 cm, and an increased hematocrit (HCT) with a concurrent decrease in platelet count ( $\leq 100,000$  platelets/mm<sup>3</sup>). The presence of comorbid conditions such as pregnancy, infancy, old age, diabetes mellitus, renal failure, or social circumstances like living alone or far from a hospital, also classifies as dengue with warning signs. Severe dengue fever was identified by severe plasma leakage leading to shock or fluid accumulation causing respiratory distress, severe bleeding as assessed by a clinician, and severe organ involvement including liver (AST or ALT  $\geq 1000$  IU/L), central nervous system (impaired consciousness), and heart or other organs. All patients were treated as per standard institutional protocols.

Data analysis was performed using "IBM-SPSS statistics, version 26.0". For quantitative variables, mean and standard deviation (SD) were calculated. Frequency and percentages were calculated for qualitative variables. Inferential statistics were explored using chi-Square or independent sample t-test taking  $p < 0.05$  as significant.

## RESULTS

Of 84 children, 48 (57.1%) were male. The mean age was  $4.58 \pm 3.48$  years (1 month to 12 years). On examination, the mean temperature, respiratory rate, and pulse rate were  $100.3 \pm 1.5$  °F,  $35.4 \pm 11.7$  respirations/min, and  $117.6 \pm 20.5$  beats/min, respectively. The mean Glasgow Coma Scale score was  $14.0 \pm 2.2$ .

Dengue fever without warning sign, dengue fever with warning sign, and severe dengue fever was diagnosed in 31 (36.9%), 30 (35.7%), and 23 (27.4%) patients, respectively. The most frequent presenting complaints were fever, nausea and vomiting, rash, and headache, reported in 80 (95.2%), 46 (54.8%), 43 (51.2%), and 36 (42.9%), respectively. Torniquet test was positive in 6

(7.1%) patients. Frequency of hepatomegaly, splenomegaly, and hepatosplenomegaly was noted in 16 (19.0%), 3 (3.6%), and 6 (7.1%) patients, respectively. The mean hemoglobin, total leukocyte count, platelets, and HCT were  $10.1 \pm 2.5$  g/dl,  $7.1 \pm 3.6$  ( $10^9/L$ ),  $74.1 \pm 79.6$  ( $10^9/L$ ), and  $39.1 \pm 12.3$  (%), respectively. Sixty eight (81.0%) children were discharged successfully, while mortality was noted in 11 (13.1%) patients. Four (4.8%) patients left against medical advice

(LAMA), and another 1 patient (1.2%) was referred to another healthcare facility. In the remaining 79 patients, mortality was significantly associated with bleeding ( $p=0.037$ ), altered mental status ( $p<0.0010$ ), and fits ( $p<0.001$ ) at initial presentation. Mortality was significantly associated with abnormal general look ( $p=0.005$ ), abnormal skin ( $p<0.001$ ), abnormal respiratory rate, and abnormal breathing pattern (Table-I).

Demographics and Clinical Characteristics		Outcome		P-Value
		Discharged (n=68)	Mortality (n=11)	
Gender	Male	38 (55.9%)	5 (45.5%)	0.519
	Female	30 (44.1%)	6 (54.5%)	
Age in Mean $\pm$ SD (years)		4.53 $\pm$ 3.60	4.87 $\pm$ 2.57	0.092
Frequency of Presenting signs and symptoms	Fever	65 (80.9%)	10 (90.9%)	0.511
	Headache	27 (39.7%)	4 (36.4%)	0.833
	Retro-orbital pain	1 (1.5%)	-	0.686
	Myalgia	12 (17.6%)	2 (18.2%)	0.966
	Bone pain	6 (8.8%)	2 (18.2%)	0.340
	Arthralgia	3 (4.4%)	2 (18.2%)	0.082
	Rash	37 (54.4%)	3 (27.3%)	0.095
	Nausea and/or vomiting	41 (60.3%)	2 (18.2%)	0.009
	Diaphoresis	1 (1.5%)	-	0.686
	Bleeding	12 (17.6%)	5 (45.5%)	0.037
	Altered mental status	7 (10.3%)	10 (90.9%)	<0.001
	Fits	13 (19.1%)	6 (54.5%)	0.011
GCS	<8	-	3	<0.001
	8-12	5	4	
	13-15	63	4	
Hypertension		6 (8.8%)	4 (36.4%)	0.011
SaO2	Normal	65 (95.6%)	9 (81.8%)	0.082
	Hypoxia	3 (4.4%)	2 (18.2%)	
Pulse pressure	Normal	65 (95.6%)	6 (54.5%)	<0.001
	Decreased	3 (4.4%)	5 (45.5%)	
General look	Stable	24 (35.3%)	-	0.005
	Lethargic	20 (29.4%)	4 (36.4%)	
	Sick	20 (29.4%)	3 (27.3%)	
	Unconscious	4 (5.9%)	4 (36.4%)	
Skin	Normal	16 (23.5%)	-	<0.001
	Pale	5 (7.4%)	7 (63.6%)	
	Cyanosis	2 (2.9%)	2 (18.2%)	
	Petechiae	42 (61.8%)	2 (18.2%)	
	Purpura	3 (4.4%)	-	
Tourniquet Test	Positive	6 (8.8%)	-	0.305
	Negative	62 (91.2%)	11 (100%)	
Respiratory rate	Normal	55 (80.9%)	5 (45.5%)	0.005
	Tachypnea	13 (19.1%)	5 (45.5%)	
	Bradypnea	-	1 (9.1%)	
Breathing	Normal	54 (79.4%)	7 (63.6%)	0.035
	Increased	14 (20.6%)	3 (27.3%)	
	Decreased	-	1 (9.1%)	

**Table-I. Association of demographic and clinical characteristics with outcome (N=79)**

Sinus bradycardia on ECG ( $p=0.007$ ) and abnormal chest x-ray ( $p=0.005$ ) were found to have significant associations with mortality. Ventilatory support was linked with significant mortality ( $p<0.001$ ). Mortality was significantly associated with SDF as 81.8% children who died had SDF ( $p<0.001$ ). Table-II shows details about the association of diagnostic and treatment related variables with outcome.

The study reveals that low hemoglobin level ( $p=0.045$ ) and platelet count ( $p=0.007$ ), increased urea ( $p<0.0010$ ), potassium ( $p=0.003$ ),

INR ( $p<0.001$ ), and APTT ( $p<0.001$ ) were found to have a significant association with mortality and the as shown in Table-III.

It was found that severe dengue fever had a significant relationship with abnormal chest x-rays ( $p<0.001$ ), ventilatory support ( $p<0.002$ ), increased hospitalization duration ( $p=0.022$ ), and mortality ( $p<0.001$ ). Table-IV shows the association of dengue classification with demographics, diagnostic variables, and outcomes.

Diagnostic and Treatment-related Variables		Outcome		P-Value
		Discharged (n=68)	Mortality (n=11)	
Blood culture	Positive	8 (11.8%)	-	0.230
	Negative	60 (88.2%)	11 (100%)	
Electrocardiogram	Normal	61 (89.7%)	7 (63.6%)	0.007
	Sinus bradycardia	4 (5.9%)	4 (36.4%)	
	Prolonged PR Interval	3 (4.4%)	-	
Chest x-ray	Normal	55 (80.9%)	7 (63.6%)	0.005
	Effusion	6 (8.8%)	1 (9.1%)	
	Infiltrate	7 (10.3%)	1 (9.1%)	
	Collapse	-	2 (18.2%)	
Dengue diagnosis	Dengue fever without a warning sign	29 (42.6%)	-	<0.001
	Dengue with warning sign	25 (36.8%)	2 (18.2%)	
	Severe dengue fever	14 (20.6%)	9 (81.8%)	
Ventilatory support		-	9 (81.8%)	<0.001
Hospital stay (days)	1-3	25 (36.8%)	8 (72.7%)	0.064
	4-7	33 (48.5%)	3 (27.3%)	
	>7	10 (14.7%)	-	

**Table-II. Association of diagnostic and treatment related variables with outcome (N=79)**

Laboratory Parameters	Outcome		P-Value
	Discharged (n=68)	Mortality (n=11)	
Hemoglobin (g/dl)	10.45±2.55	8.02±1.37	0.045
Total Leukocytes Count ( $10^9/L$ )	7.29±3.61	5.91±3.49	0.387
Platelets ( $10^9/L$ )	75.19±78.53	28.73±14.83	0.007
Hematocrit (%)	37.70±12.05	44.55±12.14	0.638
Alanine Transaminase (IU/L)	71.02±78.00	60.00±8.16	0.293
Urea (mg/dl)	22.89±14.83	47.64±33.10	<0.001
Creatinine (mg/dl)	0.71±0.46	1.44±0.50	0.281
Sodium (mEq/L)	136.11±5.80	135.09±8.29	0.087
Potassium (mEq/L)	3.90±0.70	4.16±1.21	0.003
Chlorine (mEq/L)	105.38±10.08	111.18±5.95	0.494
HCO <sub>3</sub> (mEq/L)	21.06±3.30	21.09±5.82	0.055
International normalized ratio (sec)	1.13±0.30	2.34±1.24	<0.001
Activated Partial Thromboplastin Clotting Time (sec)	28.57±7.32	77.30±86.21	<0.001

**Table-III. Association of baseline laboratory parameters with outcome (n=79)**

Study Variables		Dengue Fever Without Warning Signs (n=29)	Dengue With a Warning Sign (n=27)	Severe Severe Dengue Fever (n=23)	P-Value
Gender	Male	14 (48.3%)	15 (55.6%)	14 (60.9%)	0.657
	Female	15 (51.7%)	12 (44.4%)	9 (39.1%)	
Age (years)		4.14±3.37	5.53±3.94	4.01±2.82	0.216
Blood culture	Positive	3 (10.3%)	3 (11.1%)	2 (8.7%)	0.960
Electrocardiogram	Normal	26 (89.7%)	23 (85.2%)	19 (82.6%)	0.478
	Sinus bradycardia	2 (6.9%)	4 (14.8%)	2 (8.7%)	
	Prolonged PR Interval	1 (3.4%)	-	2 (8.7%)	
Chest x-ray	Normal	29 (100%)	22 (81.5%)	11 (47.8%)	<0.001
	Effusion	-	4 (14.8%)	3 (13.0%)	
	Infiltrate	-	1 (3.7%)	7 (30.4%)	
	Collapse	-	-	2 (8.7%)	
Ventilatory support		-	2 (7.4%)	7 (30.4%)	0.002
Hospital stay (days)	1-3	17 (58.6%)	6 (22.2%)	10 (43.5%)	0.022
	4-7	12 (41.4%)	15 (55.6%)	9 (39.1%)	
	>7	-	6 (22.2%)	4 (17.4%)	
Mortality		-	2 (7.4%)	9 (39.1%)	<0.001

**Table-IV. Association of dengue classification with demographics, diagnostic variables and outcomes (N=79)**

## DISCUSSION

Dengue fever is known to be a major public health issue in tropical as well as non-tropical countries. The spectrum of dengue fever can vary greatly across geographies, and it is important for us as a clinician to know the epidemiology of our own region to manage them appropriately. We found that 57.1% of children with dengue fever were male. A study from Bangladesh analyzing children with dengue fever during the 2019 outbreak showed that 54.5% of children were male, and our results align with these findings.<sup>10</sup> Relevant data from Southeast Asia has consistently shown that dengue fever is more common in male children.<sup>13,15</sup> The mean age of children in this study was 4.58±3.48 years. Hussain et al noted the mean age of the children with dengue fever to be 5.7±3.07 years.<sup>16</sup> Khan et al reported the mean age of children with dengue fever to be 8.8±3.7 years, which seems different to what we noted.<sup>10</sup> Variations in age distribution may occur due to regional differences, reflecting the local epidemiology of dengue. Different regions may experience distinct serotype prevalence, which can affect the age groups predominantly affected. Differences in healthcare access and infrastructure might influence the age distribution of diagnosed cases as well. Fever, nausea and vomiting, rash, headache, fits, and altered mental

status were the most frequent presentations in this study. Fever is generally considered to be the most frequent presentation of dengue fever whereas nausea vomiting, abdominal pain, are body ache are some of the most frequently reported presenting complaints.<sup>14,17</sup>

Severe dengue fever was noted in 27.4% of children in this study. Epidemiological data has shown that 33.3% of children with dengue fever are reported with SD.<sup>18</sup> Data from Columbia reported the incidence of SDF in children as 45.1%.<sup>19</sup> A study from India showed that severe dengue fever was reported in 13.4% dengue disease cases.<sup>20</sup> Differences in dengue virus serotypes, which vary in their potential to cause severe disease, play a role. The level of population immunity and previous exposure to different serotypes also impacts disease severity, with secondary infections often leading to more severe cases. Healthcare access and diagnostic practices can affect detection and reporting, with limited healthcare access potentially leading to higher reported severity due to delayed diagnosis. Regional differences in outbreak intensity and local environmental factors further contribute to these variations. Severe dengue fever was also found to be a significant predictor of mortality in our study. Severe thrombocytopenia, anemia, diminished

renal functioning and electrolyte imbalance further influences outcome among dengue fever patients and this was demonstrated clearly in the present study. Severe thrombocytopenia at the time of admission is an established risk factor for mortality among dengue fever patients.<sup>17,21</sup>

The present study reported overall mortality rates of 13.1% among children admitted with dengue fever. Contemporary literature reports mortality rates ranges between 0.7-25.6% in dengue infection.<sup>21-24</sup> Disease severity at the time of admission is the most important risk factor and directly relates to mortality. Clinicians should be vigilant in assessing the severity of dengue fever at the time of presentation and early management can improve disease outcomes.<sup>22</sup>

Being a single center study and conducted on a relatively modest sample were some of the inherent limitations of this research. The reliance on clinical and laboratory data from a single tertiary care center may not account for variations in disease presentation and management across different healthcare facilities.

## CONCLUSION

The study identified key clinical features of dengue fever in children, with common symptoms including nausea, rash, headache, and bleeding. Severe dengue, marked by sinus bradycardia, abnormal chest X-ray, and need for ventilatory support, were significantly linked to higher mortality. Early detection and intervention are crucial to improve outcomes in severe dengue cases.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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
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2	Heena Rais	Conception, Data collection, Methodology, Drafting, Critical revisions, Proof reading, Approved for publication.	
3	Tayyaba Anwer	Data collection, Methodology, Critical revisions, Proof reading, Approved for Publication.	
4	Saba Safdar	Data collection, Methodology, Critical revisions, Proof reading, Approved for Publication.	
5	Payal Bai	Data collection, Methodology, Drafting, Critical revisions, Proof reading, Approved for Publication.	