Clinical Manifestations and Factors Associated with Dengue Severity in Children in Karachi

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Abstract

Background: Dengue is a mosquito-borne viral disease. A significant number of Pakistani children are affected every year with a wide spectrum of symptoms.

Objective: To determine the frequency of the clinical features and their associated factors among pediatric patients with dengue severity at Creek General Hospital, Karachi.

Methods: This cross-sectional study was conducted in the Department of Pediatrics at Creek General Hospital, Karachi, from November 2024 to April 2025. Patients aged 1 month to 15 years with laboratory confirmation were later classified in severe and non-severe categories using the WHO 2009 guidelines. Data was analyzed using SPSS 21.

Results: A total of 154 children were included, with a mean age of 7.04 ± 3.88 years, and 79 (51.3%) were males. Severe dengue was observed in 16 (10.4%) patients. Vomiting 111 (72.1%), abdominal pain 86 (55.8%), and diarrhea 63 (40.9%) were the most common symptoms. Temperature of moderate grade 102.3-104.0'F (OR=13.46, 95% CI: 0.71-255.22), high grade fever High grade (>104 'F) (OR=230.8, 95% CI: 12.53-4255.26), stuporous consciousness level (OR=42.78, 95% CI: 1.95-938.54), dyspnea (OR=14.67, 95% CI: 4.56-47.14)), excessive sweating (OR=11.0, 95% CI:3.49-34.67), cold clammy skin (OR=67.31, 95% CI: 13.75-329.37), and thrombocytopenia (OR=12.19, 95% CI: 1.71-208.34) were significantly associated with severe dengue.

Conclusion: The findings indicate that severe dengue is associated with a higher frequency of laboratory abnormalities and more pronounced clinical manifestations. These factors were observed more commonly among patients with severe disease, highlighting their association with dengue severity and clinical outcomes.

Keywords: *Dengue, dengue hemorrhagic fever, pediatrics, thrombocytopenia, Pakistan.*

INTRODUCTION

Dengue is a mosquito-borne arboviral disease caused by the dengue virus (DENV), transmitted to humans primarily by Aedes aegypti and Aedes albopictus [1]. Dengue is common in tropical regions due to favorable environmental and climatic conditions that support large mosquito populations [2]. In Pakistan, the first significant outbreak of dengue was reported in Karachi in 1994. Sporadic cases continued until the 2005 epidemic, when several major cities were affected [3]. It remains a major public health problem in tropical and subtropical regions, including Pakistan, where recurrent outbreaks continue to place a significant burden on healthcare systems, particularly affecting the pediatric population. It has become endemic and remains a leading cause of morbidity and mortality, especially among children in Pakistan [4].

Dengue is considered the most common arboviral infection in humans worldwide, with a considerable increase in incidence in the last three decades. Indeed, recent Global Burden of Disease analyses have shown a continuing increase in dengue-related cases and disability-adjusted life years, notably in children and adolescents in low- and middle-income countries [5, 6]. The increasing geographic distribution of mosquito vectors, urbanization, population growth, and climate change have also contributed to the increased frequency and magnitude of dengue outbreaks globally [5].

Unhealthy food and improper sanitation among the population have also contributed to high mortality [7]. This virus comprises four distinct serotypes DENV-1 to DENV-4. All four serotypes have been co-circulating in Pakistan with a predominance of DENV-2 and DENV-3 in recent years. Infection with one serotype confers long-term immunity against that specific serotype but only transient cross-protection against the others. Consequently, secondary infection with a heterologous serotype may increase the risk of severe disease through immune-mediated mechanisms, including antibody-dependent enhancement. This phenomenon has been implicated in the pathogenesis of severe dengue manifestations, including plasma leakage, hemorrhage, and shock [8]. Children are particularly vulnerable to severe dengue due to their physiological and hemodynamic characteristics [9]. As a systemic disease,

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dengue presents with a wide range of clinical features, including fever, rash, vomiting, lethargy, and stupor. Severe infections are often preceded by 'warning' signs, and various laboratory findings have also been linked to disease severity [10]. The clinical spectrum of dengue ranges from an undifferentiated febrile illness to severe disease characterized by significant plasma leakage, severe bleeding, or organ dysfunction. The World Health Organization (WHO) 2009 classification categorizes dengue into dengue without warning signs, dengue with warning signs, and severe dengue, facilitating early recognition of patients at risk for clinical deterioration [11]. Several studies have identified warning signs such as persistent vomiting, abdominal pain, lethargy, hepatomegaly, rising hematocrit, and thrombocytopenia as important predictors of progression to severe disease.

Early detection and proper management of severe dengue are crucial to reducing dengue-associated mortality. Therefore, characterizing both atypical and typical clinical signs, as well as the determinants of disease severity, is essential. This study aims to determine the frequency of the clinical features and their associated factors among pediatric patients with dengue severity at Creek General Hospital, Karachi.

SUBJECTS AND METHODS

This cross-sectional study was conducted in the Department of Pediatrics at Creek General Hospital, Karachi, from November 2024 to April 2025, following approval from the ethical review committee (Ref. no. UMDC/Ethics/Ext/2024/20/372). Informed consent was obtained from the patients' parents for study participation and the use of their data in research. Both male and female patients aged 1 month to 15 years, admitted with clinical signs/symptoms and laboratory-confirmed dengue fever, were included in the study. Patients with incomplete data and those with fever due to causes other than dengue (malaria, pneumonia, typhoid) were excluded from the study.

Using the WHO sample size calculator for a single proportion, with a dengue prevalence of 24% [9], a 95% confidence level, and 7% absolute precision, the required sample size was calculated as 154. A non-probability consecutive sampling approach was employed. Data was extracted directly from medical records by the researchers using a standardized form to minimize collector bias.

Based on the World Health Organization (WHO) 2009 guidelines, patients [10] were categorized as follows: Dengue fever + warning signs were classified as 'non-severe dengue,' defined by the presence of at least 2 clinical findings in a febrile individual who resides in or has traveled to a dengue-endemic area within the past 14days. Clinical findings include nausea, vomiting, rash, aches and pains, a positive tourniquet test, leukopenia, or any warning sign such as persistent vomiting, mucosal bleeding, abdominal pain or tenderness, clinical fluid accumulation, lethargy, restlessness, and liver enlargement >2cm, increase in HCT concurrent with rapid decrease in platelet count.

"Severe dengue" was defined as dengue accompanied by any of the following clinical manifestations: severe bleeding, impaired consciousness, or heart impairment, severe plasma leakage leading to shock or fluid accumulation with respiratory distress; or severe organ impairment such as hepatitis (elevated transaminases ≥1,000 IU/L). Non-consenting patients or those with other confirmed causes of fever were excluded from the study.

A concise history was obtained from the parent regarding the demographic profile, duration of the illness, and the presence or absence of clinical parameters, and was entered into the form by the researcher. A blood sample was collected and sent for CBC, electrolytes, and liver function tests.

All data was entered in an Excel worksheet. Data analysis was performed using SPSS 21, in which the mean and standard deviation were computed for continuous variables such as age, weight, and duration of fever, and percentages and frequencies were calculated for qualitative variables such as clinical parameters and gender. Stratification was performed by age, gender, duration of fever, and other factors. The Chi-square test, Fisher's Exact test, or Fisher-Freeman-Halton exact test was employed to assess the association between patients' features and dengue severity. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for selected key clinical severity markers. No multivariable analysis was performed because of the limited number of severe dengue cases. P-value <0.05 was considered as statistically significant.

RESULTS

A total of 154 children were included in the study. 79 (51.3%) were males. Mean±SD age of study populations was 7.04 + 3.8 years, mean weight was 20.42 + 7.4 kg, mean duration of fever was 6.40 + 3.0 days, and mean duration of hospital stay was 5.40 + 3.3 days. By severity, 16 (10.4%) children had severe dengue, while the rest had non-severe dengue. The majority of children, 62 (40.3%), were in the 6-10-year age group—all presented with fever. Vomiting was the commonest gastrointestinal symptom found in 111 (72.1%), followed by abdominal pain and diarrhea. children. A very small percentage of patients suffered from hematuria, nasal bleeding, or mucosal bleeding. 128 (83.1%) had a normal level of consciousness, while only 2 (1.3%) were in stupor. Children classified as having severe dengue more frequently exhibited prolonged fever, longer hospital stay, higher body temperature, dyspnea, cold, clammy skin, excessive sweating, and altered level of consciousness, all of which are recognized clinical manifestations of severe dengue according to WHO criteria, as presented in Table **1**.

Table 1: Comparison of general demographics, clinical presentation between non-severe and severe dengue cases.

Variables	Non-severe n(%)	Severe Dengue n(%)	Total n(%)	p-value	Odds ratio (95% CI)
Age					
Up to 5 years	53 (38.4)	3 (18.8)	56 (36.4)	0.144*	
6-10 years	52 (37.7)	10 (62.5)	62 (40.3)		-
11-15 years	33 (23.9)	3 (18.8)	36 (23.4)		
Weight					
1-10kg	28 (20.3)	1 (6.3)	29 (18.8)		
11-20kg	50 (36.2)	10 (62.5)	60 (39.0)	0.091*	-
21-30kg	52 (37.7)	3 (18.8)	55 (35.7)		
31-40kg	8 (5.8)	2 (12.5)	10 (6.5)		
Hospital Stay					
1-7 days	116 (84.1)	4 (25.0)	120 (77.9)	<0.001†	15.82 (4.67-53.58)
>7 days	22 (15.9)	12 (75.0)	34 (22.1)		Ref
Duration of Fever					
1-7 days	108 (78.3)	4 (25.0)	112 (72.7)	<0.001†	10.80(3.25-35.92)
>7 days	30 (21.7)	12 (75.0)	42 (27.3)		Ref
Temperature Grading					
Low grade (100.4-102.2'F)	78 (56.5)	0 (0.0)	78 (50.6)	<0.001*	Ref
Moderate grade (102.3-104.0'F)	52 (37.7)	4 (25.0)	56 (36.4)		13.46 (0.71-255.22) (Moderate *vs* Low Grade)
High grade (>104 'F)	8 (5.8)	12 (75.0)	20 (13.0)		230.8(12.53-4255.26) (High *vs* Low grade)
Headache					
Yes	42 (30.4)	4 (25.0)	46 (29.9)	0.778†	0.76 (0.23-2.50)
No	96 (69.6)	12 (75.0)	108 (70.1)		Ref
Retrobulbar Pain					
Yes	26 (18.8)	5 (31.3)	31 (20.1)	0.241	1.96 (0.62-6.16)
No	112 (81.2)	11 (68.8)	123 (79.9)		Ref
Nausea					
Yes	26 (18.8)	0 (0.0)	26 (16.9)	0.075	0.13 (0.007-2.23)
No	112 (81.2)	16 (100)	128 (83.1)		Ref
Rash					
Yes	59(42.8)	6(37.5)	65(42.2)	0.687	0.80 (0.28-2.32)
No	79(57.2)	10(62.5)	89(57.8)		Ref
Muscle Pain					
Yes	50(36.2)	7 (43.8)	57 (37.0)	0.555	1.37 (0.49-3.82)
No	88(63.8)	9 (56.3)	97 (63.0)		Ref
Joint Pain					
Yes	13(9.4)	3 (18.8)	16 (10.4)	0.221†	2.22 (0.56-8.73)
No	125(90.6)	13 (81.3)	138(89.6)		Ref
Vomiting					
Yes	99(71.7)	12 (75.0)	111 (72.1)	0.989†	1.18 (0.36-3.91)
No	39(28.3)	4 (25.0)	43 (27.9)		
Abdominal Pain					
Yes	78(56.5)	8 (50.0)	86 (55.8)	0.619	0.77 (0.28-2.13)
No	60 (43.5)	8 (50.0)	68(44.2)		Ref
Diarrhea					
Yes	58 (42.0)	5 (31.3)	63 (40.9)	0.406	0.63 (0.22-1.80)
No	80(58.0)	11 (68.8)	91 (59.1)		Ref
Constipation					
Yes	25(18.1)	4 (25.0)	29 (18.8)	0.505†	1.51 (0.46-4.94)
No	113(81.9)	12 (75.0)	125(81.2)		Ref
Abdominal Tenderness					
Yes	52 (33.8)	7 (4.5)	59 (38.3)	0.787	1.29 (0.45-3.66)
No	86(55.8)	9 (5.8)	95 (61.7)		Ref
Mucosal Bleed					
Yes	28(20.3)	1(6.3)	29(18.8)	0.309†	0.26 (0.03-2.05)
No	110(79.7)	15(93.7)	125(81.2)		Ref

Variables	Non-severe n(%)	Severe Dengue n(%)	Total n(%)	p-value	Odds ratio (95% CI)
Nasal Bleed					
Yes	11 (8.0)	1 (6.3)	12 (7.8)	1.000†	0.77 (0.09-6.57)
No	127 (92.0)	15 (93.8)	142 (92.2)		Ref
Hematemesis					
Yes	2 (2.2)	5 (31.3)	7 (4.5)	0.156	23.75 (4.08-138.18)
No	133 (97.8)	14 (68.8)	147 (95.5)		Ref
Hematuria					
Yes	3 (1.9)	1 (6.3)	4 (2.6)	0.358†	3.00 (0.29-30.86)
No	135 (87.7)	15 (93.8)	150 (97.4)		Ref
Lethargy					
Yes	45 (32.6)	7 (43.8)	52 (33.8)	0.409	1.61 (0.58-4.50)
No	93 (67.4)	9 (56.3)	102 (66.2)		Ref
Level of Consciousness					
Normal	115 (83.3)	13 (81.3)	128 (83.1)	<0.005*	Ref
Irritable	9 (6.5)	1 (6.3)	10 (6.5)		0.98(0.12-8.39)
Lethargic	14 (10.1)	0 (0.0)	14 (9.1)		0.30(0.02-5.23)
Stuporous	0 (0.0)	2 (12.5)	2 (1.3)		42.78(1.95-938.54)
Dyspnea Present					
Yes	18 (13.0)	11(68.8)	29 (18.8)	<0.001	14.67(4.56-47.14)
No	120 (87.0)	5(31.3)	125 (81.2)		Ref
Excessive Sweating					
Yes	23 (16.7)	11(68.8)	34 (22.1)	<0.001	11.0(3.49-34.67)
No	115 (83.3)	5\(31.3)	120 (77.9)		Ref
Cold Clammy Skin					
Yes	13 (9.4)	14 (87.5)	27 (17.5)	<0.001†	67.31(13.75-329.37)
No	125 (90.6)	2(12.5)	127 (82.5)		Ref

†:Fisher's Exact test, *Fisher-Freeman-Halton exact test, CI: Confidence interval, Ref: Reference category

Odds ratios were reported for selected key clinical severity markers to illustrate the magnitude and direction of their associations with severe dengue. The analysis identified cold, clammy skin and high-grade fever as being associated with severe dengue. Other significant associations with high odds ratios included hospital stays exceeding 7 days, dyspnea, excessive sweating, and fever duration over 7 days. A lower but significant association was observed regarding levels of consciousness. These estimates should be interpreted with caution, given the small number of severe dengue cases, as shown in Table **1**. In this cohort, thrombocytopenia was significantly associated with severe dengue. All patients with severe dengue had

Table 2: Comparison of laboratory parameters between non-severe and severe dengue cases.

Variables	Non-severe n(%)	Severe Dengue n(%)	Total n(%)	p-value	Odds ratio (95% CI)
Increased Hematocrit					
Yes	15 (10.9)	3 (18.8)	18 (11.7)	0.404†	1.89(0.48-7.41)
No	123 (89.1)	13 (81.3)	136 (88.3)		Ref
Leucopenia (<4000/mm³)					
Yes	44 (31.9)	5 (31.3)	49 (31.8)	1.000†	0.97(0.32-2.96)
No	94 (68.1)	11 (68.8)	105 (68.2)		Ref
Thrombocytopenia (<150,000/mm³)					
Yes	101 (73.2)	16 (100)	117 (76.0)	0.013†	12.19(1.71-208.34)
No	37 (26.8)	0 (0.0)	37 (24.0)		Ref
Dengue Tests					
NS1 Antigen Positive	36 (26.1)	6 (37.5)	42 (27.3)	0.410*	-
Serology Positive	78 (56.5)	9 (56.3)	87 (56.5)		1.44(0.48-4.37) (NS1 *vs* Serology)
Both Positive	24 (17.4)	1 (6.3)	25 (16.2)		0.36(0.04-3.00) (Both Positive *vs* Serology)
SGPT					
Normal	38 (27.5)	5 (31.3)	43 (27.9)	0.985	0.84(0.27-2.57)
Increased	100 (72.5)	11 (68.8)	111 (72.1)		Ref

*Fisher-Freeman-Halton exact test, †: Fisher's Exact test, CI: Confidence interval, Ref: Reference category,

thrombocytopenia, and the association was statistically significant (p=0.013), indicating a very strong link, as shown in Table **2**.

DISCUSSION

Dengue is a common febrile illness in Pakistani children. In our study, 62 (40.3%) children were between 6 and 10 years old, and 79 (51.3%) were male. Similar findings were reported by Khan *et al.* [12]. A higher proportion of male children has also been reported in studies conducted in other South Asian countries [13, 14]. We observed that 15(10.32%) children suffered from severe dengue. Afroze *et al.* [15] have reported a higher number of severe cases (one-fifth of cases). This could be due to differences in dengue peak seasonal patterns.

All patients presented with fever, and 78 (50.6%) had low-grade fever (100.4-102.2°F). It was also noted that high-grade fever was more commonly associated with severe dengue. The mean duration of hospital stay was 5.40 ± 3.33 days. This was slightly higher than the 3.8 days reported by a researcher in India [16]. Gastrointestinal symptoms such as nausea, vomiting, and diarrhea were commonly observed in our study. Vomiting was highly prevalent in both non-severe and severe cases. Diarrhea was more prevalent than constipation. This is consistent with a previously conducted study [17]. Other symptoms, such as headache, retrobulbar pain, and joint pain, were less commonly reported.

When we analyzed various bleeding manifestations (including mucosal bleeding, nasal bleeding, hematemesis, and hematuria) among children with non-severe and severe dengue, we found that the frequency of nasal bleeding was similar in both groups. There was a higher proportion of mucosal bleeding in non-severe cases than in severe cases. Hematemesis was slightly more common in severe cases compared to non-severe cases. The frequency of hematuria was low in both groups. Mucosal bleeding was the commonest bleeding manifestation in 29 (18.8%) cases. Slightly different findings have been reported by a researcher, who found nasal bleeding to be the commonest bleeding manifestation, followed by Malena [18]. None of the bleeding manifestations showed significant differences between non-severe and severe dengue cases in our study population. Lethargy was more commonly observed in non-severe cases and was not a distinguishing factor for severity in this cohort. Normal consciousness was predominant in non-severe cases. Children with severe dengue were more likely to exhibit altered levels of consciousness, such as irritability and stupor, compared to non-severe cases. Dyspnea was significantly more prevalent in severe cases (p-value < 0.001), indicating it is a critical symptom for identifying severe dengue. Respiratory distress should prompt immediate medical attention and evaluation for severe dengue. Excessive sweating occurred significantly more often among patients with severe dengue (p-value < 0.001). Cold, clammy skin occurs at a rate that exceeds double that in other cases (p-value < 0.001), thereby establishing this symptom as an essential indicator of disease severity. It may indicate poor perfusion and impending shock, requiring urgent intervention. Similar findings have been reported by Htun *et al.* [10]. These findings are expected, as these features form part of the WHO diagnostic criteria for severe dengue and therefore represent manifestations of disease severity rather than independent predictors.

Increased hematocrit was slightly more prevalent in non-severe cases. The p-value of 0.353 suggests no significant difference between non-severe and severe cases. This indicates that increased hematocrit, although a known marker in dengue, was not a distinguishing factor for severity in our cohort. Leucopenia is a common feature of dengue, but does not strongly correlate with disease severity in this study population. Thrombocytopenia is commonly seen in patients with dengue and may be due to virus-induced bone marrow hypoplasia affecting bone marrow progenitor cells [19, 20]. Thrombocytopenia was significantly more common in severe cases (p-value = 0.017). This result indicates that thrombocytopenia was more commonly observed in children with severe dengue, reflecting its well-recognized role as a laboratory manifestation of advanced disease, and monitoring platelet levels is crucial for assessing disease progression and risk. We found that although positive dengue serology tests are essential for diagnosis, they do not differ significantly between non-severe and severe cases (p-value of 0.410).

The study has several major restrictions: first, the research results are from a single hospital, so they should be treated with caution. We used only Chi-square testing; multivariable modeling to control for the effects of age, illness duration, and baseline laboratory results was not employed because of the limited number of children with severe dengue. So, multivariable regression analysis was not done. The results of this study should be treated as exploratory and descriptive rather than as evidence of independent predictors. The severe dengue group had only 15 patients, which increased the risk of a Type I statistical error. The study lacked sufficient statistical power to identify independent relationships between variables and disease severity; researchers must treat statistically significant results as uncertain.

CONCLUSION

In conclusion, fever occurred in every case of severe dengue. The observation of dyspnea, cold, clammy skin, altered consciousness, thrombocytopenia, and electrolyte imbalance occurred more frequently in severe dengue patients, which proves the need to monitor these specific symptoms continuously. These insights are crucial for improving the clinical management and outcomes of dengue-affected children in Pakistan.

ETHICS APPROVAL

Ethics approval was obtained from the ethical review committee of United Medical and Dental College, Karachi, Pakistan (Ref. no. UMDC/Ethics/Ext/2024/20/372). All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and the Declaration of Helsinki.

CONSENT FOR PUBLICATION

The study was conducted after obtaining formal written consent from the patient's parents/guardians.

AVAILABILITY OF DATA

Authors confirm that data supporting the results of this study are available in the article. Data can be provided on request.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Declared none.

AUTHORS' CONTRIBUTION

Study conception was given by SH. Study was designed by SH, MHM, FS, ES, FA and MA. Data was collected by ES and FA. Data was analyzed by MA. Manuscript drafting was done by MHM, FS, ES, FA and MA. The manuscript was critically reviewed and revised by SH. All authors read and approved the final version of the manuscript.

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