

The Profile and Outcome of Dengue Patients Admitted to a Pediatric Intensive Care Unit of Chittagong Medical College Hospital Chattogram, Bangladesh during 2022 Outbreak

Muhammad Javed Bin Amin Chowdhury^{1*}
Dhiman Chowdhury¹
Zabeen Choudhury¹
Mir Mosharof Hossain²
Syeda Humaida Hasan²
Aparup Kanti Das¹
Kamrun Nahar¹
Munmun Chowdhury¹

¹Department of Pediatrics
Chittagong Medical College Hospital
Chattogram, Bangladesh.

²Department of Neonatology
Chittagong Medical College Hospital
Chattogram, Bangladesh.

Abstract

Background: Bangladesh is among the countries reporting regular outbreaks of Dengue infection recently. An alarming surge in dengue among Bangladeshi children has created an enormous burden in morbidity and mortality. This study aimed to document the profile, outcome and associated factors of clinical outcomes of dengue patients admitted to the PICU of a tertiary-level hospital in Chattogram, Bangladesh, during the 2022 outbreak.

Materials and methods: This prospective observational study was performed among children with dengue infection who were admitted to the PICU of Chittagong Medical College Hospital from 1st August 2022 to 31st December 2022. Clinical features, laboratory parameters and outcome of transfer from ICU to ward or death were studied and described.

Results: The patients' Median (IQR) age was 5.0 (1.5-10.5). Most patients were urban dwellers (69.6%); 56.5% were male. Common findings during admission were persistent vomiting (60.9%), lethargy (52.2%), positive tourniquet test (78.3%), and hypotension (69.6%). Dengue shock syndrome and dengue hemorrhagic fever were diagnosed in 56.4% and 30.5% of the patients. The median length of stay in the PICU was 4 (3-6) days. The overall outcome revealed that 78.5% of patients were improved and discharged, and 21.5% died in the PICU. In univariate analysis, factors associated with PICU mortality were younger age, altered level of consciousness, lethargy, shock and prolonged CRT at admission ($p < 0.05$). All of the deceased cases had dengue shock syndrome.

Conclusion: One out of every five PICU-admitted dengue cases expired. A multi-center study with a large sample size must have a clear picture of the predictors of poor outcomes.

Key words: Children; Clinical outcome; Dengue; Pediatric ICU.

INTRODUCTION

Dengue is endemic in Bangladesh, and this country is currently grappling to control its most devastating dengue fever outbreak recorded since the dengue virus reappeared in the country in 2000.^{1,2} In the last year, a total of 61,732 dengue cases and 281 dengue-related deaths were reported in Bangladesh and the 2022 outbreak was the third-largest outbreak since 2000.³ In 2022, Bangladesh had an unexpected long dengue incidence and increased death, which might be due to like prolonged intermittent rain, late reporting of patients to the hospital at an afebrile critical phase, reinfection by different strains of Dengue virus etc.^{4,5}

Dengue has a wide spectrum of clinical presentation, often with unpredictable clinical evolution and outcome.⁶ Most patients have a self-limiting non-severe clinical course, and a small proportion progress to severe disease, mostly

*Correspondence to:
Dr Muhammad Javed Bin Amin Chowdhury
Assistant Professor
Department of Pediatrics
Chittagong Medical College
Chattogram, Bangladesh
Mobile : +88 01674 30 28 39
Email : javedbinamin@yahoo.com

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characterized by plasma leakage with or without hemorrhage.⁶ Previous studies conducted in Pediatric Intensive Care Unit (PICU) in Bangladesh and in neighbouring countries showed high case fatalities and prolonged hospitalization in critically ill dengue children.⁷⁻¹⁰ Several factors can contribute to the patients' outcomes in PICU and clinical type, delayed recognition of warning signs along with delayed referral to PICU, acute kidney injury, acute liver injury, encephalitis, fluid overload percentage, shock condition at PICU admission may be responsible for such outcome.⁷⁻¹⁰

Previously, we have studied the clinical profile and outcome of hospitalized children with dengue fever during 2019 and 2022 outbreaks.¹¹⁻¹⁴ Studies on clinical outcomes of children with severe dengue treated in the PICU are still limited while findings from studies in other settings may not be applicable in our setting. The wide practice of unsafe traditional medications in combination with limited access to PICU facilities may have implications for the care of children with severe dengue in the Bangladeshi setting. Furthermore, the complexity of the referral system for critically ill children are often cause delays in treatment. This study aimed to evaluate the clinical outcomes of patients with dengue admitted to our PICU during 2022 and its associated factors. Such knowledge would be useful to clinicians for targeting at-risk groups of severe dengue for initiating prompt interventions to save lives.

MATERIALS AND METHODS

This prospective observational study was conducted in PICU of Chittagong Medical College Hospital, Chattogram, Bangladesh from August 2022 to December 2022. Ethical approval was obtained from the Ethical Review Committee of Chittagong Medical College. Informed consent was obtained from the parents or caregivers of the patients.

All the children below 12 years of age having clinical features of dengue and confirmed by IgM, or rapid dengue test NS1Ag were included in the study. Children with other diseases were excluded from the study.

Data regarding demographic characteristics, clinical features, vital parameters, laboratory features were collected by using a structured case record form during admission to PICU. Patients were followed-up daily to record the outcome in terms of PICU mortality and length of stay in PICU. For every patient, the follow-up period ended when the outcome, death or PICU discharge was reached. Patients were classified and treated as per the national guideline.¹⁵

Data processing and analysis were carried out using the Statistical Package for the Social Sciences (SPSS), Version 23.0 (IBM Corp., Chicago, Illinois, USA). Categorical variables are presented as counts and percentages. Continuous data are presented as mean and Standard Deviation (SD) for normally distributed data or median and quartile (Q) Q1 and Q3 for skewed data. Patients were categorized into two groups: survivor and non-survivors. Categorical variables were

compared either by Chi-square test or Fisher's exact test and quantitative variables by Mann-Whitney U test. P value <0.05 was considered as statistical significance.

RESULTS

From August 2022 to December 2022, a total of 23 children age between 1 month to 12 years were admitted to the PICU. Out of them 18 patients were discharged from PICU and 5 patients expired giving the PICU mortality rate of 21.7%. Table I shows that, overall, there were 56.5% males and 43.5% females. Near about half of the subjects were in childhood age (47.8%) and most of the patients were from urban area (69.6%). Median age of the deceased subjects were significantly lower and 3 out of 5 (60%) deceased subjects were infant.

Table I Demographic characteristics of the PICU admitted dengue patients

Variables	Deceased (n=5)	Survived (n=18)	Total (n=23)	p value
Age, years				
≤1 year	3 (60.0)	1 (5.6)	4 (17.4)	0.017**
>1 year-5 year	1 (20.0)	7 (38.9)	8 (34.8)	
>5 year	1 (20.0)	10 (38.9)	11 (47.8)	
Median (IQR)	0.9 (0.5-4.3)	6.5 (2.0-11.0)	5.0 (1.5-10.5)	0.030†
Sex				
Male	3 (60.0)	10 (55.6)	13 (56.5)	1.0*
Female	2 (40.0)	8 (44.4)	10 (43.5)	
Residence				
Rural	2 (40.0)	5 (27.8)	7 (30.4)	0.621*
Urban	3 (60.0)	13 (72.2)	16 (69.6)	

Data were expressed as frequency (%) or median (Interquartile range). **Chi-square test, †Mann-Whitney U test, *Fisher's exact test.

Regarding presenting symptoms during admission in PICU, persistent vomiting was the most frequent complain (60.9%) followed by lethargy (52.2%). On examination, positive tourniquet test was the most frequent finding (78.3%) followed by hypotension (69.6%). Table II shows that, altered level of consciousness, lethargy, shock, and prolonged CRT was significantly more common among deceased subjects than the survivors (p<0.05).

Table II Clinical characteristics of the PICU admitted dengue patients

Variables	Deceased (n=5)	Survived (n=18)	Total (n=23)	p value*
Fever	2 (40.0)	5 (27.8)	7 (30.4)	0.641
Headache	1 (20.0)	6 (33.3)	7 (30.4)	1.0
Abdominal pain	1 (20.0)	4 (22.2)	5 (21.7)	1.0
Persistent vomiting	4 (80.0)	10 (55.6)	14 (60.9)	0.611
Myalgia	1 (20.0)	4 (22.2)	5 (21.7)	1.0
Backpain	1 (20.0)	5 (27.8)	6 (26.1)	1.0

Variables □	Deceased □ (n=5)	Survived □ (n=18)	Total □ (n=23)	p value*
Diarrhoea □	2 (40.0) □	5 (27.6) □	7 (30.4) □	0.621
Retro-orbital pain □	1 (20.0) □	3 (16.7) □	4 (17.4) □	1.0
Skin rash □	1 (20.0) □	5 (27.8) □	6 (26.1) □	1.0
Bleeding spot □	3 (60.0) □	4 (22.2) □	7 (30.4) □	0.142
Mucosal bleeding □	2 (20.0) □	1 (5.6) □	3 (13.0) □	0.107
ALC □	4 (80.0) □	2 (11.1) □	6 (26.1) □	0.008
Convulsion □	3 (60.0) □	3 (16.7) □	6 (26.1) □	0.089
Lethargy □	5 (100.0) □	7 (38.9) □	12 (52.2) □	0.037
Less urine output □	2 (40.0) □	1 (5.6) □	3 (13.0) □	0.107
Shock □	5 (100.0) □	3 (16.7) □	8 (34.8) □	0.002
Dehydration □	2 (40.0) □	6 (33.3) □	8 (34.8) □	1.0
Hypotension □	5 (100.0) □	11 (61.1) □	16 (69.6) □	0.272
Narrow pulse pressure □	1 (20.0) □	3 (16.7) □	4 (17.4) □	1.0
Positive tourniquet test □	5 (100.0) □	13 (72.2) □	18 (78.3) □	0.545
Prolonged CRT □	5 (100.0) □	3 (16.7) □	8 (34.8) □	0.002
Organomegaly □	1 (20.0) □	1 (5.6) □	2 (8.7) □	0.395
Oedema □	2 (40.0) □	2 (11.1) □	4 (17.4) □	0.194
Pleural effusion □	0 (0) □	2 (11.1) □	2 (8.7) □	1.0
Ascites □	1 (20.0) □	2 (11.1) □	3 (13.0) □	0.539
Sign of fluid overload □	0 (0) □	1 (5.6) □	1 (4.3) □	1.0
Associated medical conditions □	2 (40.0) □	9 (50.0) □	11 (47.8) □	1.0

Data were expressed as frequency (%), *Fisher's exact test, ALC: Altered Level of Consciousness CRT: Capillary Refill Time (CRT) > 3 second

Hematological and biochemical parameters of the subjects at admission are shown in Table III. It shows that, median hemoglobin level and lymphocyte percentage in blood was significantly lower among deceased subjects than the survivors ($p < 0.05$).

Table III Laboratory features of the PICU admitted dengue patients

Variables □	Deceased (n=5) □	Survived (n=18) □	Total (n=23) □	p value
Hb, gm/dl □	8.7 (8.6-10.5) □	11.1 (9.9-12.3) □	10.5 (9.1-11.7) □	0.031†
Hematocrit (%) □	28.4 (25.1-31.6) □	31.7 (30.0-36.9) □	31.4 (28.4-36.0) □	0.055†
Leukocyte count, $\times 10^9/L$ □	5.7 (4.5-10.9) □	8.1 (6.3-10.8) □	7.7 (6.0-10.4) □	0.199†
Neutrophil (%) □	62.0 (60.0-74.0) □	58.0 (55.8-68.3) □	60.0 (57.0-69.0) □	0.130†
Lymphocyte (%) □	19.0 (18.0-32.0) □	36.0 (28.7-38.0) □	34.0 (25.0-37.0) □	0.037†
Thrombocytopenia □	3 (60.0) □	7 (38.9) □	10 (43.5) □	0.618*
ALT, U/L □	78.0 (36.5-103.5) □	43.5 (30.3-86.0) □	45.0 (34.0-86.0) □	0.491†
S. Creatinine, mg/dl □	0.9 (0.5-2.7) □	0.5 (0.4-0.7) □	0.5 (0.4-0.7) □	0.094†
S. Sodium, mmol/L □	139 (135-157) □	137 (133-141) □	138 (134-141) □	0.363†
S. Potassium, mmol/L □	4.3 (3.6-5.4) □	4.2 (3.8-4.7) □	4.2 (3.8-4.8) □	0.587†
S. Chlorine, mmol/L □	102 (97.5-117.5) □	101 (97.7-102.0) □	101 (98-102) □	0.638†
S. HCO_3 , mmol/L □	18.0 (16.6-21.5) □	21.6 (19.8-23.1) □	21.0 (19.0-23.0) □	0.080†

Data were expressed as median (Interquartile range) or frequency (%). # <150,000 mm^3 . †Mann-Whitney U test, *Fisher's exact test.

Out of 23 children, 56.5%, 30.4%, and 13% were labeled as DSS, DHF, and DF with associated medical conditions. Median starting fluid was 10 ml/kg/min and median length of ICU stay was 4 days in the study. All of the deceased cases were DSS in the study.

Table IV Dengue clinical type, starting intravenous fluid, and length of ICU stay of the PICU admitted dengue patients

Variables □	Deceased □ (n=5)	Survived □ (n=18)	Total □ (n=23)	p value
Clinical type □	□	□	□	
□ Dengue shock syndrome □	5 (100.0) □	8 (44.4) □	13 (56.5) □	0.086 □
□ Dengue hemorrhagic fever □	0 (0) □	7 (38.9) □	7 (30.4) □	
□ DF with associated disease □	0 (0) □	3 (16.7) □	3 (13.0) □	
Starting iv fluid, ml □	□	□	□	
□ Median (IQR) □	10.0 (10.0-20.0) □	7.5 (5.0-12.5) □	10.0 (5.0-20.0) □	0.094†
PICU stay, days □	□	□	□	
□ Median (IQR) □	4.0 (0.7-5.5) □	4.0 (3.0-6.5) □	4.0 (3.0-6.0) □	0.415†

Data were expressed as frequency (%) or median (Interquartile range). Chi-square test, †Mann-Whitney U test.

DISCUSSION

Rapid identification of severe cases and appropriate clinical management remains the mainstay to avoid dengue-related case fatalities. However, there is a wide variation among the clinical presentation of dengue infection, outcome and its predictors especially in severe dengue, the present study was designed to address these issues.¹⁶ All of the 23 seropositive patients admitted to PICU of a tertiary center in Southeast Bangladesh during August 2022 to December 2022 were analyzed. Thirteen (56.4%) and seven (30.5%) patients had DSS and DHF, respectively. Male: female ratio was 1.3:1, which was comparable to that of earlier reports by Bhaskar et al.¹⁰ and Palaniappan et al.¹⁷ In both of these studies male to female ratio was exactly 1.3:1. Commonest age group in the present study was 5-12 years. Akhter et al. Bhaskar et al. and Palaniappan et al. showed a similar finding with common age group being 5-10 years.^{7,10,17}

Previous studies found that fever was the most common presenting symptom among the PICU admitted dengue children at admission to PICU.^{7,10,17} In contrast, fever was present in only 7 (30.4%) patients in the present series during their PICU admission. Common findings during admission were persistent vomiting (60.9%), lethargy (52.2%), positive tourniquet test (78.3%), and hypotension (69.6%) in the present study. Other than fever, the common clinical feature was hypotension (84.1%), narrow pulse pressure (72.2%) in the study of Akhter et al.⁷ Pain abdomen was found to be the second most common symptom, being present in 85.7% cases, followed by vomiting which was present in 74.2% cases in the study of Bhaskar et al.¹⁰ Vomiting was the second most common clinical feature and was present in 56.8% of patients followed by abdomen

pain and reduced urine output in 32.7% in the study of Palaniappan et al.¹⁷ This discrepancy in symptomatology may be due to the difference in the patients severity and clinical types of the individual studies. In the present study pleural effusion and ascites was present in 8.7% and 13% of the patients, respectively. Akhter et al. found that 26.2% patients had both pleural effusion and ascites. Isolated pleural effusion present in 17.5% cases.⁷

Case fatality rate in this study was 21.7%, which was comparable to study by Kumar et al. (21%) and Akhter et al. (21.43%).^{8,7} However, present mortality rate was comparatively higher than the study of Bhaskar et al. (8.6%) and Palaniappan et al. (12.1%).^{10,17} Other than the small sample size, this discrepancy in case fatality rate may be due to the difference in the patients characteristics and management facilities. In the current study, median (IQR) length of PICU stay was 4 (3-6) days. Akhter et al. found that the mean duration of hospital stay was 7.83 (± 3.0) days, whereas Bhaskar et al. found that the duration was 5.5 days in Dengue without co-infection and 11.8 with co-infection.^{7,10}

A recent systematic review and meta-analysis reported that being a child, secondary dengue infection, pre-existing comorbidities and warning signs were the main predictors of severe dengue.¹⁷ However, studies addressing the predictors of mortality in pediatric patients were scarce. Due to the small sample size, it was impossible to do an extensive analysis to this end. The present study identified that PICU mortality was associated with younger age, altered level of consciousness, lethargy, shock and prolonged CRT at admission. Use of inotropes and mechanical ventilation are associated with higher mortality in the study of Bhaskar et al. and Palaniappan et al.^{10,17}

LIMITATIONS

There were some limitations to the consideration of our study. Our setting still uses manual medical records. We tried to minimize all data collection error by adding a second data collector who validated the data input process. This study was also a single-center study with a small sample size, that might not reflect the overall situation of critically ill pediatric dengue patients in Bangladesh. Moreover, we were not able to consider the role of secondary dengue infection, viremia, and dengue virus serotypes in this study.

CONCLUSION

Case fatality rate was 21.7% among critically ill PICU admitted dengue children. Mortality was common in the age group of <1 year and in DSS. Significantly more no. of children who died had altered level of consciousness, lethargy, shock, and prolonged CRT at admission.

RECOMMENDATION

Considering the increasing dengue cases in our country, a multi-center study with large sample size is urgently needed to have clear picture regarding the predictors of poor outcome in critically ill children with dengue infection.

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DISCLOSURE

The authors declared no conflicts of interest.

REFERENCES

1. □ Haider N, Asaduzzaman M, Hassan MN, Rahman M, Sharif AR, Ashrafi SA, Lee SS, Zumla A. Bangladesh's 2023 Dengue outbreak—age/gender-related disparity in morbidity and mortality and geographic variability of epidemic burdens. *International Journal of Infectious Diseases*. 2023; 136 (2023):1-4.
2. □ Hossain MS, Noman AA, Mamun SM, Mosabbir AA. Twenty-two years of dengue outbreaks in Bangladesh: epidemiology, clinical spectrum, serotypes, and future disease risks. *Tropical Medicine and Health*. 2023;51(1):1-4.
3. □ Ministry of Health and Family Welfare (Management Information System). Daily Press release on dengue outbreak. Dhaka: DGHS. 2023. <https://old.dghs.gov.bd/index.php/bd/home/5200-daily-dengue-status-report>.
4. □ Islam QT. Prolonged Period of Dengue Season is Unexplained. *Bangladesh Journal of Medicine*. 2023;34(1):1-3.
5. □ Roy MG, Uddin K, Islam D, Singh A, Islam MM. All four-dengue virus serotypes co-circulate in concurrent dengue infections in a single dengue session in Chittagong, Bangladesh. *Bioresearch Communications*. 2022;8(1):1042-1048.
6. □ World Health Organization, Special Programme for Research, Training in Tropical Diseases, World Health Organization. Department of Control of Neglected Tropical Diseases, World Health Organization. Epidemic, Pandemic Alert. Dengue: guidelines for diagnosis, treatment, prevention and control. World Health Organization. 2009.
7. □ Akhter RJ, Paul SP, Ahmed F. Outcome of Dengue Patients Admitted in the PICU of Bangladesh Shishu Hospital & Institute. *Dhaka Shishu (Children) Hospital Journal*. 2021;37(2):103-108.
8. □ Kumari P, Yadav R, Pareet R, Meena SC. Pattern of clinical presentation, lab findings and mortality risk among patients of dengue fever admitted in pediatric intensive care unit in a tertiary care centre in South-east Rajasthan. *International Journal of Health Sciences*. 2022;6(S2):12425–12435.
9. □ Armenda S, Rusmawatiningsy D, Makrufardi F, Arguni E. Factors associated with clinical outcomes of pediatric dengue shock syndrome admitted to pediatric intensive care unit: A retrospective cohort study. *Annals of Medicine and Surgery*. 2021;66:102472.
10. □ Bhaskar V, Hemrom J, Kumar V, Kumar S, Chhapola S. Clinical profile and outcome of critically sick patients of dengue, admitted in PICU of a tertiary care center. *J Pediatr Crit Care*. 2016;3(4):20-24
11. □ Ahmed FU, Datta M, Aktar NJ. Comparison of Clinical Features and Outcome of Dengue Infection Between Children and Adults: A Hospital Based Study. *Journal of Rangamati Medical College*. 2020; 3(1):2-6.
12. □ Datta M, Ferdousi A, Haque S, Jahan R, Das A, Haq T. Dengue Outbreak in Children During 2019: Experience at A Tertiary Care teaching Hospital. *Chattagram Maa-O-Shishu Hospital Medical College Journal*. 2021;20(1):46-50.
13. □ Das AK, Choudhury Z, Chowdhury MJBA, Shil S, Datta M, Das S, et al. Differences in Clinical Profiles and Outcomes of Children with Dengue During the 2019 and 2022 Outbreaks: Experience from a Tertiary Hospital, Chattogram, Bangladesh. *Journal of Chittagong Medical Teachers Association*. 2023; 34(1):116-120.
14. □ Chowdhury P, Hoque S, Choudhury Z, Chowdhury MJBA, Shil S, Das AK. Clinical spectrum and outcome of children with dengue admitted to a tertiary-level hospital in Bangladesh during the 2022 outbreak. *Journal of Rangamati Medical College*. 2023; 6(1):2-5.
15. □ National guideline for clinical management of dengue syndrome. 4th ed. Dhaka: Government of the People's Republic of Bangladesh. 2018;87.
16. □ Tsheten T, Clements AC, Gray DJ, Adhikary RK, Furuya-Kanamori L, Wangdi K. Clinical predictors of severe dengue: a systematic review and meta-analysis. *Infectious diseases of poverty*. 2021;10(1):1-10.
17. □ Palaniappan A, Mani N, Krishnamoorthi N. Clinical profile and outcome of dengue in children admitted in pediatric intensive care unit in a tertiary center in South India. *Journal of Pediatric critical Care*. 2018;5:15-21.