



Clinical Profile, Laboratory Findings and Outcome of Severe Dengue Infection among Children Admitted at a Tertiary Care Hospital in Bangladesh

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Abstract

Background: Dengue infection is endemic in Bangladesh and presents with varying degrees of severity of illness in children. **Objective:** The purpose of the present study was to assess the common clinical profile, biochemical findings and outcome of severe dengue fever in children. **Methodology:** This prospective cohort study was conducted on dengue NS1 or IgM or RT-PCR positive admitted children up to 14 years of age from April 2019 to October 2019 for a period of 6 months at the Pediatrics Department of Evercare Hospital, Dhaka. Data were analyzed after collection of demographic variables, presenting complaints and examination findings of 75 enrolled children. Detailed clinical examination, serial monitoring of vital sign was done for all patients. Serial monitoring of hemogram, liver function tests, renal function tests, coagulation profile, serum electrolytes, chest X-ray were performed. All patients were managed according to management protocol of national guideline⁴. In refractory shock extended measures (inotropes, 3% NaCl) were taken. Outcome measured was either recovery or death. **Results:** A total of 75 cases were classified as severe dengue fever. The most common age of presentation was 4 to 7 years. The most common presenting symptom of severe dengue cases were fever (97.3%), abdominal pain and vomiting (77.3%) and shock (62.7%). Pleural effusion was the most common physical findings seen in 35(46.6%) cases followed by ascites in 26(34.7%) cases. Elevation in aspartate amino transaminase AST (IU/L) was found in 82.6% cases, low albumin was found in 78.7% cases. Hyponatremia was the most common electrolyte abnormality found in 35(46.7%) cases. Regarding coagulation profile, raised D-dimer and low fibrinogen was found in 53 (70.7%) and 42 cases (56.0%) respectively. Activated partial thromboplastin time (aPTT) was prolonged in 37.3% cases. Case fatality rate (CFR) was 5.3% cases. **Conclusion:** In conclusion, raised AST and D-dimer, low fibrinogen and albumin level as well as hyponatremia are significant laboratory findings indicating severity of the disease. [*Bangladesh Journal of Infectious Diseases, December 2022;9(2):40-46*]

Keywords: Dengue fever; clinical profile; severe dengue infection

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Introduction

In Bangladesh, the first outbreak of dengue fever was documented in 1964 in Dhaka; the first epidemic of Dengue hemorrhagic fever (DHF) occurred in mid-2000, when 5,551 dengue infections were reported from different cities mainly affecting adults; the case fatality rate was reported 1.7% with 93 deaths¹. Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas. Case fatality rate was 12.1% cases among severe dengue. Severe capillary leak with refractory shock unresponsive to any therapy is the common cause of death in dengue.

The 2019 dengue outbreak in Bangladesh is a nationwide occurrence of dengue fever that began primarily in April 2019. After the incubation period of 4 to 10 days, the infected *Aedes aegypti* mosquito is capable of transmitting the virus for the rest of its life. The infection causes a flu-like illness and occasionally develops into a potentially lethal complication called severe dengue. The global incidence of dengue has grown dramatically in recent decades. About 3.9 billion people, in 128 countries, are at risk of infection with dengue viruses. Even though most often dengue fever presents with self-limiting mild illness, severe dengue infection increases morbidity and few of them succumb to serious complications and death. Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas.

Severe dengue is a leading cause of severe illness and death among children in some Asian and Latin American countries. The exact clinical and laboratory profile is crucial for diagnosis as well as the successful management of the patients². In Asia, high number of cases were reported in Bangladesh (101,000), Malaysia (131,000) Philippines (420,000), Vietnam (320,000)³. Aim of this study was to observe the common clinical features, laboratory findings of severe dengue fever as well as their final outcome in children which could help to early detection of complications and thus could help to reduce the morbidity and mortality.

Methodology

Study Settings and Population: This prospective cohort study was conducted from April 2019 to October 2019 for a period of 6 months at the Pediatrics Department of Evercare Hospital. The hospitalized children aged up to 14 years

irrespective of sex with positive dengue tests, either NS1 antigen, IgM antibody or RT-PCR test were included in the study. Children with other bacterial & parasitic illness, neonate were excluded from the study.

Study Procedure: Purpose of the study was explained to the parents. Informed consent as obtained from all the parents before conducting the study. Dengue case classification by severity was done as per national guidelines of dengue fever Bangladesh 2019. Demographic variables, presenting complaints and examination findings were recorded on a structured questionnaire. Detailed clinical examination, serial monitoring of vital sign was done for all patients. Serial monitoring of hemogram, liver function tests, renal function tests, coagulation profile, serum electrolytes, chest X-ray were performed. All patients were managed according to management protocol of national guideline⁴. In refractory shock extended measures (inotropes, 3% NaCl) were taken. Outcome measured was either recovery or death.

Statistical Analysis: The statistical analysis was carried out using the Statistical Package for Social Sciences version 22.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Qualitative variables like gender, classification, blood group, clinical features were expressed as frequency and percentage; quantitative variables like age, duration of hospitalization and ICU stay were expressed as mean \pm standard deviation.

Ethical Clearance: All procedures of the present study were carried out in accordance with the principles for human investigations (i.e., Helsinki Declaration) and also with the ethical guidelines of the Institutional research ethics. Formal ethics approval was granted by the local ethics committee.

Results

The common age group was 4-7 years which was near about one third of total patient (34.7%). The mean age was 7.9 ± 3.7 years. Youngest one was 1 month of age. In this study male patients were predominant than female patients which were 40 (54.36 %) and 34 (45.3%) respectively. Male female ratio was 1.2:1. It was observed that half of the patients (53.3%) had normal weight followed by obese (25.3%), overweight (17.3%) and 4% patients were underweight. B+ ve blood group was found in 37.3% patients followed by O+ ve (29.3%), A+ ve (26.7%) and AB+ ve were 2.7% (Table 1).

Table 1: Distribution of the Study Patients by Demographic Profile (n=75)

Demographic Profiles	Frequency	Percent
Age Group		
• ≤3 Years	10	13.3
• 4 to 7 Years	26	34.7
• 8 to 11 Years	25	33.3
• >11 Years	14	18.7
Mean ±SD	7.9±3.7	
Range (min-max)	0.2-16	
Gender		
• Male	40	54.3
• Female	34	45.3
Weight for age		
• Normal	40	53.3
• Under weight	3	4
• Over weight	13	17.3
• Obese	19	25.3
Blood group		
• A+	20	26.7
• AB+	2	2.7
• B+	28	37.3
• O+	22	29.3

The total numbers of cases of severe dengue were 75, out of which dengue shock syndrome (DSS) was 52.0% of the patients followed by dengue hemorrhagic fever (DHF) in 17.3% of patient and expanded dengue syndrome (EDS) was 10.7% cases. Sixteen percent patient of DSS progressed to DHF and 4.0% patient of DHF progressed to grade EDS after admission and hospital stay (Table 2).

Table 2: Distribution of the Study Patients by classification(n=75)

Classification	Frequency	Percent
DSS	39	52.0
DHF	13	17.3
EDS	8	10.7
DSS with DHF	12	16.0
DHF with EDS	3	4.0

DSS= Dengue shock syndrome; DHF=Dengue hemorrhagic fever; EDS= Expanded dengue syndrome

In this study, 57 (76.0%) patients were positive for NS1 followed by 14 (18.7%) cases IgM, 15 (20.0%) cases RT-PCR, 7 (9.3%) cases IgG and IgM, 10 (13.3%) cases NSI and RT-PCR, 6 (8.0%) cases both NSI and IgM (Table 3).

Table 3: Diagnosis of Dengue Cases

Dengue Serology Positive	Frequency	Percent
NS1	57	76.0
IgM	14	18.7
RT-PCR	15	20.0
IgG & IgM	7	9.3
NSI & RT-PCR	10	13.3
NSI & IgM	6	8.0

Most common symptom was fever seen in 97.3% during admission. It was observed that more than half (56.0%) patients had duration of fever 4 to 6 days followed by ≤3 days in 27 (36.0%) cases and >6 days in 4 (5.3%) cases. Most common symptom was abdominal pain & vomiting which was more than three fourth (77.3%) of patients followed by shock in 47(62.7%) of patients. Rash was found in 14 (18.7 %) cases. It was observed that 12 (16.0%) cases had loose stool, 12 (16.0%) cases had breathing difficulty and 6 (8.0%) cases had cough. Headache was present in 5 cases (6.7%) cases, myalgia & arthralgia in 4 (5.3%) cases. Convulsion and altered consciousness was rare presentation seen in 3 (4.0%) cases and 2 (2.7%) cases respectively. Pleural effusion was most common physical findings seen in 35 (46.6%) cases followed by ascites in 26 (34.7%) cases then 16 (21.3%) cases had hepatomegaly. Bleeding manifestation was seen in 21.2% of patients. The most common bleeding manifestation was hematemesis and melena in 12(16.0%) cases followed by prick site bleeding in 2(2.7%) cases, gum bleeding in 1(1.3%) case and menorrhagia in 1(1.3%) case (Table 4).

Table 4: Clinical Presentation of Severe Dengue Cases

Clinical Features	Frequency	Percent
Duration of Fever	73	97.3
Less than 3 days	27	36.0
4 to 6 days	42	56.0
More than 6 days	4	5.3
Abdominal pain & vomiting	58	77.3
Shock	47	62.7
Ascites	26	34.7
Pleural effusion	35	46.6
Hepatomegaly	16	21.3
Rash	14	18.7
Loose stool	12	16.0
Breathing difficulty	12	16.0
Cough	6	8.0
Headache	5	6.7
Myalgia & Arthralgia	4	5.3
Convulsion	3	4.0

Clinical Features	Frequency	Percent
Altered consciousness	2	2.7
Splenomegaly	0	0.0
Bleeding	15	21.3
Hematemesis and melena	12	16.0
Prick site bleeding	2	2.7
Gum bleeding	1	1.3
Menorrhagia	1	1.3

Among the liver enzymes, AST (IU/L) or SGOT was elevated in a larger proportion 82.6% of patients when compared to raised ALT or SGPT which was 65.3% of patients. Low albumin was found in 59 (78.7%) cases which was one of the parameters of severity. Parameters like prothrombin time (PT) and activated partial thromboplastin time (aPTT) were prolong in 34.7% cases and 37.3% cases respectively. Raised D-dimer & low fibrinogen was found in 70.7% & 56.0% of patients respectively which were indicator of dengue severity like DHF. Six (8.0%) cases had raised creatinine. Regarding electrolytes hypernatremia was most common findings found in 35 (46.7%) cases followed by hypokalemia in 14 (18.7%) cases, hyperkalemia in 3 (4.0%) cases hypernatremia in 3 (4.0 %) cases. Raised D-dimer and low fibrinogen was found in 70.7% and 56.0% of patients respectively which were indicator of dengue severity like DHF. Pleural effusion was found in 50.7% of the cases detected by chest X-ray. Right sided effusion was most commonly seen which 42.7% cases followed by was left sided effusion in 6.7% cases, bilateral effusion in 1.3% of the cases. Among these severe dengue cases, 33.3% cases had pulmonary edema, 1.3% cases had pericardial effusion (Table 5).

Table 5: Laboratory Parameters of Severe Dengue Cases

Parameters	Frequency	Percent
Leukopenia (<4000cells/mm ³)	21	28.0
Thrombocytopenia	64	85.3
Raised Hematocrit (>45%)	20	26.7
Raised ALT (IU/L)	49	65.3
Raised AST (IU/L)	68	82.6
Low Albumin	59	78.7
Prolong PT	26	34.7
Prolong APTT	28	37.3
Raised Creatinine	6	8.0
Hypokalemia	14	18.7
Hyperkalemia	3	4.0

Parameters	Frequency	Percent
Hyponatremia	35	46.7
Hypernatremia	3	4.0
Raised D-dimer	53	70.7
Low fibrinogen	42	56.0
Chest X-ray		
• Right pleural effusion	32	42.7
• Left pleural effusion	5	6.7
• Bilateral pleural effusion	1	1.3
• Pulmonary edema	25	33.3
• Pericardial effusion	1	1.3

Average duration of hospital stay was 4 to 6 days in 61.3% of patients. The mean duration was 4.8±2 days with range 1 to 14 days. ICU care was required in 98.7% of the patients and average ICU stay was ≤3 days in 80.0% of patients. The mean ICU stay was 2.2±2 days, with ranged from 1 to 8 days. In our study majority 71 (94.7%) cases recovered, 4 (5.3%) cases expired due to intractable shock, multi organ failure and DIC (Table 6).

Table 6: Outcomes of Severe Dengue Cases

Outcomes	Frequency	Percent
Duration of Hospitalization		
• Less than 3 days	18	24.0
• 4 to 6 days	46	61.3
• More than 6 days	10	13.3
Mean ±SD	4.8±2	
Range (min-max)	1-14	
ICU stay (in)		
• ≤3 days	44	80.0
• 4-6 days	11	14.7
• >6 days	3	4.0
Mean ±SD	2.2±2	
Range (min-max)	1-8	
Recovery	71	
Death	4	

Discussion

Clinical presentation has a wide variation in severe dengue fever as well as their laboratory parameter. We designed the present study to address the common sign and symptoms and frequency of findings of common deranged laboratory parameter of severe dengue so that we can predict and manage the cases timely and appropriately.

The mean age of the study participants was 7.9±3.7 years, range from 4 to 7 years. Male female ratio was 1.2:1. Similar results were reported by the

study done by Pothapregada et al⁵ and Hoque et al². Pothapregada found mean age was 6.9 ± 3.3 years, male: female ratio was 1.2:1 and Hoque found common age group of 5-10 years, female ratio was 1.3:1. In this study, more than half (52.0%) patients had DSS during admission followed by 17.3% in DHF and 10.7% in EDS. Sixteen percent patient of DSS progressed to DHF and 4.0% patient of DHF progressed to EDS after admission and during hospital stay. Rosenberger et al⁶ showed similar findings that severe vascular leakage occurred in 244 (90%), severe bleeding in 39 (14%), and severe organ dysfunction in 28 (10%) of 271 severe dengue patients. ICU care needed in 98.7% of the patients and average ICU stay was ≤ 3 days in 80.0% of patients. However, Mishra et al⁷ reported 63.9% of patients were admitted in the ICU for 3–6 days.

Fever was the most common clinical feature and was present in 97.3% patients who are comparable to the earlier observations whereas Pothapregada et al⁵ reported fever in 94.6% cases, Aggarwal et al⁸ reported fever in 93% patients and Daniel et al⁹ reported fever in 96.8% of patients. Abdominal pain & vomiting were the second most common clinical feature and was present in 77.3% patients which is like other reports. Daniel et al⁹, Bhave et al¹⁰ reported abdominal pain as second most clinical features followed by vomiting. Adam¹¹ reported shock (15.7%), mucosal bleeding (36.4%), clinical fluid accumulation (15%), shortness of breath (14.3%) and vomiting were commonly presented in SD while mucosal bleeding, clinical accumulation of fluid was most common warning sign in SD. In this study we found rash in 14(18.7%) cases and Shock in 47(62.7%) cases which were prominent feature of SD. Srivastava¹³ found shock in 70.8% of patients. The most common bleeding manifestation was hematemesis and melena in 12(16.0%) cases which was supported by the study done by Srivastava¹² and Ahmed et al¹³. Srivastava has reported 90.0% cases, Ahmed has reported 61.0% cases GIT hemorrhages. Pleural effusion was most common physical findings seen in 35(46.6%) cases followed by ascites in 26(34.7%) cases then 16(21.3%) cases had hepatomegaly. But other study by Pothapregada et al⁵, Mishra et al⁷, Ahmed et al¹³, Joshi et al¹⁴ where hepatomegaly was the most common physical finding.

Normal leukocyte count was present in 63.54% cases, while leucopenia was seen in 21(28%) cases which were consisted with other studies^{7,13}. However, Ratageri et al¹⁵ showed leukopenia was significantly related with severe dengue cases which was against our result. It was shown that

among the liver enzymes, AST was elevated in a larger proportion in 45(60%) cases, these findings were similar with the study done by Mishra et al⁷ where they found AST was elevated in 47.4% patients when compared to alanine aminotransferase (ALT) which was 30.92% cases. Low albumin was found in 59(78.7%) cases, which was almost similar with the value (72.8%) obtained by Ferreira, et al¹⁶, however, much higher than the value (33%) obtained by Thyagaraj et al¹⁷ and Relwani et al¹⁸. Pleural effusion was found in 50.7% cases detected by chest X-ray. Right sided effusion was most commonly seen which 42.7% followed by was left sided effusion in 6.7% of cases which was consistent with study done by Mishra et al⁷ right sided effusion (15.46%) was most commonly seen followed by bilateral effusion (6.18%). In this study hyponatremia was found in 35 cases (46.7%) followed by hypokalemia in 14(18.7%) cases were most common electrolyte abnormalities which was consistent with the study Relwani et al¹⁸ where hyponatremia was found in 45.33% and hypokalemia in 10.60% of cases. Shankar et al¹⁹ also reported that hyponatremia and hypokalemia were common electrolyte abnormalities. Serum electrolytes testing early is very important in dengue patients during management so that if abnormalities are found, they can be appropriately managed as some of these abnormalities may lead to increased severity. Khalil et al²⁰ showed coagulopathy as a significant risk factor for mortality. Raised D-dimer and low fibrinogen was found in 70.7% cases and 56.0% cases respectively which are indicator of dengue severity like DHF whereas Sridhar et al²¹ showed significantly higher D-dimer levels in DHF patients compared with DF patients with the sensitivity of D-dimer in predicting DHF of 90.0%. DD was also found to be positively correlated with dengue severity in all stages of disease namely febrile, toxic and convalescent (P-value <0.05). In consistence with this study raised D-dimer & low fibrinogen was found in 70.7% cases and 56.0% patients respectively. In our study we found 26(34.7%) cases had prolonged PT, 28(37.3%) cases had prolonged aPTT which was higher than the Balakrishnan et al²² where 20.9% cases had prolonged PT and 33.3% cases had prolonged aPTT.

The common blood group in this study was B positive which was in 37.3% patients. Similar result was found in the study done by Khode et al²³ found common blood group O positive 42.8% cases. Joshi et al²⁵ found common blood group was O positive and B group is more prevalent in children which was similar with our study. In this study, 25.3%

patients were obese, 17.3% patients were overweight. Almost all obese and overweight patients were presented with DSS. Kurnia et al²⁴ reported that prevalence of DHF with shock is fifty per cent's and DHF without shock was 50% cases. Prevalence of obesity was 40.9% cases and the severity of DHF was significantly correlated with P-value 0.004. In our study majority of the cases (94.7%) were recovered. We observed 5.3% cases death in severe dengue in our study. Among 4 patients who were died three of them were obese; develop DIC with multi organ failure. The rest one had severe acute asthma with sepsis with intractable shock. However recently published article by Hoque et al² in Dhaka city showed case fatality rate was 12.1% cases among severe dengue. There are some limitations of the present study. The study of dengue fever cases from a single center and included only those cases that were admitted to the hospital. No control groups. The diagnosis was confirmed by either dengue NS1 antigen test or dengue serology and PCR. Viral isolation and serotype identification were not done in the present study.

Conclusion

In conclusion, severe dengue is one of the dreaded fever for the paediatric age group. Despite varied presentations, some symptoms and signs may help identify severity of the disease early. Abdominal pain & vomiting with ascities & pleural effusion were predominant features of severe disease. Raised AST & D-dimer, low fibrinogen & albumin level as well as hyponatremia are significant laboratory findings indicating severity of the disease. Early suspicion and effective management can improve outcome and reduce mortality of the disease.

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Conflict of Interest

No conflict of interest

Financial Disclosure

The author(s) received no specific funding for this work. All the costing are personal.

Contribution to authors

Jannatul Ferdous designed the overall study; Jannatul Ferdous & Badrun Nessa were responsible for data collection; Jannatul Ferdous, Laila Nurun Nahar involved in data cleaning; Janatul Ferdous, Farzana Nahid conducted data analysis and interpretation. Jannatul Ferdous drafted the first manuscript; Quamrul Hassan, Sabina Sultana, Nurun Naher revised the manuscript. All authors read and approved the final manuscript.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the Institutional Review Board. Informed consent was not obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

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