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Original Research Article

Clinical profile and prognosis of severe dengue infection in pediatric population admitted to tertiary care hospital

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ABSTRACT

Background: Dengue fever is one of the most important emerging vector-borne viral diseases. Approximately 500,000 out of 100 million cases develop severe dengue infection. Dengue infection is endemic to Bangladesh and presents with varying degrees of severity of illness in Bangladeshi children. Objectives was to assess the common clinical profile, biochemical findings associated with severe dengue fever, and their outcome in children less than 14 years of age.
Methods: This was an observational study conducted from April 2022 to October 2022 at the Pediatrics Department of Dhaka Medical College Hospital and Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
Results: A total of 150 cases were classified as severe dengue. The most common age of presentation was 6-8 years. The most common presenting symptom was fever (97.3%) followed by abdominal pain and vomiting (77.3%) followed by shock in 94 cases (62.7%) of severe dengue. Pleural effusion was the most common physical finding seen in 70 cases (46.6%) followed by ascites in 52 cases (34.7%). Elevation in aspartate transaminase AST (IU/L) was found in 60.0%, low albumin was found in 78.7% of the cases. Hyponatremia was the most common electrolyte abnormality found in 70 cases (46.7%). Regarding coagulation profile raised D-dimer and low fibrinogen were found in 106 cases (70.7%) and 84 cases (56.0%) respectively. Activated partial thromboplastin time (aPTT) was prolonged in 37.3% of cases. The case fatality rate (CFR) was (5.3%).
Conclusions: Abdominal pain and vomiting, shock, as-cities and pleural effusion were dominant features of severe disease. Raised AST and D-dimer, low fibrinogen and albumin level as well as hyponatremia are very significant findings in severe disease. Early suspicion and effective management can reduce the severity.

Keywords: Clinical profile, Dengue fever, Predictors for mortality, Severe dengue cases

INTRODUCTION

Dengue fever (DF) was first reported in Dhaka, Bangladesh in 1964. The first epidemic of dengue hemorrhagic fever (DHF) occurred in the mid-2000s, when 5,551 cases were reported across various cities, primarily affecting adults. During this epidemic, the case fatality rate was 1.7%, with 93 reported deaths.[1] The 2019 dengue outbreak in Bangladesh is a nationwide occurrence of dengue fever that began primarily in April 2019.[2] High number of cases were reported in Bangladesh (101,000), Malaysia (131,000) Philippines (420,000), Vietnam (320,000) in Asia (WHO 2019).[3] World Health Organization (WHO) has considered it a major global health problem, due to its impact on the healthcare system worldwide.[4] Globally, dengue fever (DF) is endemic in >100 countries including Bangladesh.[5] Dengue has a variety of clinical presentations, ranging

from completely asymptomatic to mild clinical features to high-grade fever with viral syndrome or in the severest forms as dengue hemorrhagic fever (DHF) which can even be fatal. The most common clinical presentation of DF is an acute febrile viral disease with headaches, bone, joint and muscular pains, rash, and leucopenia.[6]

The clinical manifestations of dengue infection range from mild febrile illness (i.e., DF) to severe hemorrhagic disease (i.e., DHF) and Dengue Shock Syndrome (DSS).[7,8] Classical dengue patients usually present with fever, arthralgia, myalgia, retro-orbital pain, and rash. Dengue cases also present with hemorrhagic manifestation (e.g. sub-conjunctival hemorrhage, petechiae, epistaxis, etc.) with or without shock. Respiratory symptoms, gastrointestinal disorders, reduced platelet count, and abnormal liver function tests were also evident as presenting features of dengue now a day.[9] A temporal variation in the frequency of different clinical manifestations can be noted over the decade since the first outbreak.[10-14] For example the outbreak of 2000 and 2002 were characterized by high-grade fever with typical purpuric rash, break-bone body ache, and thrombocytopenia, whereas in 2010 and 2018 outbreaks, predominant manifestations were fever, gastrointestinal symptoms and bleeding manifestation with normal platelet counts.[15] Frequent transitions to plasma leakage leading to respiratory distress syndrome and organ dysfunction were more commonly observed and were considered a predicting factor of higher case fatality.

Clinical diagnosis of dengue can be challenging, depending largely on what stage in the infection process a patient presents. Depending on the geographic region of the world, there can be a number of disease-causing pathogens or disease states that can mimic the disease spectrum arising from dengue infection. In the early stages of clinical disease, dengue can present as a mild undifferentiated “flu-like” fever with symptoms similar to those of other diseases such as influenza, measles, Zika, chikungunya, yellow fever, and malaria.[16] Correct diagnosis of the pathogen responsible for the later manifestation of shock is of particular importance, as a treatment for dengue-induced shock vs that arising from sepsis traditionally requires different approaches. However, a potential, paradigm-shifting observation that DENV infection activates similar innate immune pathways as those induced in sepsis may suggest alternative, common targets for treatment.[17] Because the clinical symptoms of dengue are so diverse, accurate clinical diagnosis is challenging. As such, it is essential that laboratory or point-of-care diagnostics be used in conjunction with the assessment of clinical presentation. Dengue fever is known to affect hematological and biochemical parameters and a simple clinical and laboratory monitoring of the affected patients helps to reduce the morbidity and mortality. Patients with severe dengue (SD) can be predicted by clinical profile, laboratory and warning signs which could be saved by early interventions. To validate this hypothesis the present study is aimed to assess the common clinical symptoms, and laboratory findings of severe dengue fever as well as their final outcome in children up to 14 years of age in Dhaka city where dengue outbreaks are rampant during 2019.

METHODS

The cross-sectional observation-based study was conducted on 150 children admitted to the Department of Pediatrics of Dhaka Medical College Hospital and Bangabandhu Sheikh Mujib Medical University in Dhaka, Bangladesh, with severe dengue infection between April 2022 and October 2022. Dengue case classification by severity was done as per national guidelines of dengue fever Bangladesh 2019. Dengue case classification by severity was done as per national guidelines of dengue fever Bangladesh 2019 [18]. The observation-based study was approved by the institutional ethical committee and by legal guardians.

Inclusion criteria

All children aged up to 14 years with positive dengue tests, either NS1 antigen, IgM antibody, or RT-PCR test with severe dengue fever were included in the study.

Exclusion criteria

Children with other bacterial and parasitic illnesses were excluded from the study. Demographic variables, presenting complaints, and examination findings were recorded on a structured questionnaire. Serial monitoring of vital signs was done and recorded from all patients. Serial monitoring of hemograms, liver function tests, renal function tests, coagulation profiles, serum electrolytes, and chest X-rays was performed. All patients were managed according to the standards management protocol of national guidelines [18]. In refractory shock, extended measures (inotropes, 3% Nacl) were given. The 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). Descriptive statistics were done for quantitative data as a minimum and maximum of the range as well as mean ± SD (standard deviation) for quantitative normally distributed data, while it was done for qualitative data as number and percentage. Inferential analyses were done for quantitative variables using an independent t-test in cases of two independent groups with normally distributed data. In qualitative data, inferential analyses for independent variables were done using the Chi-square test for differences between proportions. The level of significance was taken at P value <0.050 as significant, otherwise non-significant. Qualitative variables are expressed as frequency, percentage like gender,

classification, blood group, and clinical features, and quantitative variables like age, duration of hospitalization, and ICU stay are expressed as mean±standard deviation

RESULTS

The common age group was 6-8 years which was near about one-third of total patients (30.7%). The mean age was 5.56±3.57 years.

The youngest one was 1 month of age. Fifty-four (54.7%) percent of patients were male and 45.3% of patients were female. The male-female ratio was 1.2:1. It was observed that half of the patients (53.3%) maintained their normal weight followed by obese (25.3%), overweight (18.7%), and 2.7% of patients were underweight (Table 1).

Table 1: Demographic distribution of the study patients (n=150).

Demographic profile	Number of patients	Percentage
Age in years		
≤2	14	9.3
03-05	36	24
06-08	46	30.7
09-11	38	25.3
>11	16	10.7
Mean±SD	5.56 ± 3.57	
Gender		
Male	82	54.7
Female	68	45.3
Weight (kg)		
Normal	80	53.3
Underweight	4	2.7
Overweight	28	18.7
Obese	38	25.3

The average duration of hospital stay was 4 to 6 days in 62.7% of patients. The mean duration was 4.8±2 days with a range of 1 to 14 days. The average ICU stay was ≤3 days in 58.7% of patients. The mean ICU stay was 2.2±2 days, ranging from 1 to 8 days. The total number of cases of severe dengue were 150, out of which dengue shock syndrome (DSS) was in 52.0% of the patients followed by dengue hemorrhagic fever (DHF) in 17.3% of patient and expanded dengue syndrome (EDS) was 10.7% of the patient. 16.0% of patients with DSS progressed to DHF and 4.0% of patients with DHF progressed to grade EDS after admission and hospital stay. B+ ve blood group was found in 37.3% of patients followed by O+ ve (29.3%), A+ ve (26.7%) and AB+ ve were 2.7% (Table: 2).

The most common symptom was fever seen in 97.3% during admission. It was observed that more than half (56.0%) of patients had a duration of fever of 4-6 days followed by ≤3 days in 54 cases (36.0%) and ≥7 days in 8 cases (5.3%). The next most common symptom was abdominal pain and vomiting which were more than three fourth (77.3%) of patients followed by shock in 94 (62.7%) of patients. The rash was found in 28 cases (18.7%). It was observed that 24 cases (16.0%) had loose stool, 24 cases (16.0%) had breathing difficulty and 12 cases (8.0%) had a cough. Headache was present in 10 cases (6.7%), myalgia and arthralgia in 8 cases (5.3%). Convulsion and altered consciousness were rare presentations seen in 6 cases (4.0%) and 4 cases (2.7%) respectively. Pleural effusion was the most common physical finding seen in 70 cases (46.6%) followed by ascites in 52 cases (34.7%) then 32 cases (21.3%) had hepatomegaly. The bleeding manifestation was seen in 21.3% of patients. The most common bleeding manifestation was hematemesis and melena in 24 cases (16.0%) followed by prick site bleeding in 4 cases (2.7%), gum bleeding in 2 cases (1.3%), and menorrhagia in 2 cases (1.3%) (Table 3).

Table 2: Distribution of the study patients after hospitalization (n=150).

Distribution of the study	Number of patients	%
Duration of hospitalization (in days)		
≤3	36	24
04-06	94	62.7
>6	20	13.3
Mean±SD	4.8±2	
ICU stay (in days)		
≤3	88	58.7
04-06	56	37.3
≥6	6	4
Mean ±SD	2.2±2	
Range (min-max)		1-8
Classification		
Dengue shock syndrome DSS	78	52
Dengue hemorrhagic fever DHF	26	17.3
Expanded dengue syndrome EDS	16	10.7
DSS with DHF	24	16
DHF with ED	6	4
Blood group		
A+	40	26.7
AB+	4	2.7
B+	62	41.3
O+	44	29.3

In our study, three fourth (76.0%) patients were positive for NS1 followed by 28 cases (18.7%) IgM, 30 cases (20.0%) RT-PCR, 14 cases (9.3%) IgG and IgM, 20 cases (13.3%) NSI and RT-PCR, 12 cases (8.0%) both NSI and IgM. Among the liver enzymes, AST (IU/l) or SGOT was elevated in a larger proportion of 60.0% of patients when compared to raised ALT or SGPT which was 42.7% of

patients. Low albumin was found in 118 cases (78.7%), which was almost similar to the value (72.8%) obtained by but much higher than the value (33%) obtained by which was one of the parameters of severity.

Table 3: Clinical presentation of severe dengue cases.

Clinical presentation	Number of patients	Percentage
Fever		
Duration of fever (in days)	146	97.3
≤3	54	36
04-06	84	56
>6	8	5.3
Clinical features		
Abdominal pain and vomiting	116	77.3
Shock	94	62.7
Ascites	52	34.7
Pleural effusion	70	46.6
Hepatomegaly	32	21.3
Rash	28	18.7
Loose stool	24	16
Breathing difficulty	24	16
Cough	12	8
Head ache	10	6.7
Myalgia and Arthralgia	8	5.3
Convulsion	6	4
Altered consciousness	4	2.7
Splenomegaly	0	0
Bleeding	30	20
Hematemesis and melena	24	16
Prick site bleeding	4	2.7
Gum bleeding	2	1.3
Menorrhagia	2	1.3

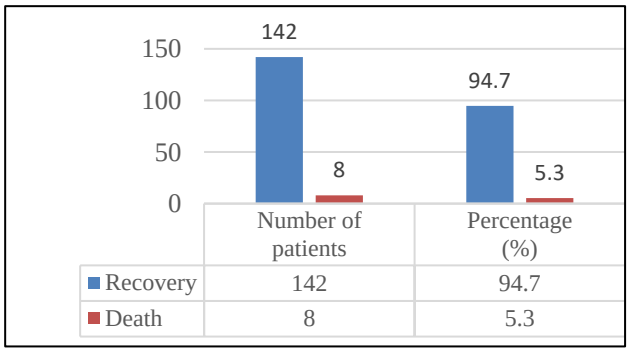

Figure 1: Outcome of severe dengue cases.

Parameters like prothrombin time (PT) and activated partial thromboplastin time (aPTT) was prolonged in 34.7% and 37.3% of cases respectively. Raised D-dimer and low fibrinogen was found in 70.7% and 56.0% of patients respectively which were an indicator of dengue severity like DHF. Six (8.0%) cases had raised creatinine. Regarding electrolytes, hyponatremia was the most common finding found in 70 cases (46.7%) followed by hypokalemia in 28 cases (18.7%), hyperkalemia in 6 cases (4.0%) hypernatremia in 6 cases (4.0%).

Table 4: Investigations of severe dengue cases.

Investigations	Number of patients	Percentage
Dengue serology		
NSI	114	76
IgM	28	18.7
RT-PCR	30	20
IgG and IgM	14	9.3
NSI and RT-PCR	20	13.3
NSI and IgM	12	8
Leukopenia (<4000cells/mm3)	42	28
Thrombocytopenia	128	85.3
Raised Hematocrit (>45%)	40	26.7
Raised ALT (IU/L)	64	42.7
Raised AST (IU/L)	90	60
Low Albumin	118	78.7
Prolong PT	52	34.7
Prolong APTT	56	37.3
Raised Creatinine	12	8
Hypokalemia	28	18.7
Hyperkalemia	6	4
Hyponatremia	70	46.7
Hypernatremia	6	4
Raised D-dimer	106	70.7
Low fibrinogen	84	56
Chest X-ray		
Right pleural effusion	64	42.7
Left pleural effusion	10	6.7
Bilateral pleural effusion	2	1.3
Pulmonary edema	50	33.3
Pericardial effusion	2	1.3

Raised D-dimer and low fibrinogen was found in 70.7% and 56.0% of patients respectively which were an 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 in 42.7% followed by left-sided effusion in 6.7% of cases, and bilateral effusion in 1.3% of the cases. Among these severe dengue cases, 33.3% of cases had pulmonary edema, and 1.3% cases had pericardial effusion (Table 4).

In our study, the majority of 142 cases (94.7%) recovered, and 8 cases (5.3%) expired due to intractable shock, multi-organ failure, and DIC (Figure 1).

DISCUSSION

The clinical presentation has a wide variation in severe dengue fever as well as their laboratory parameter. By identifying the common signs, symptoms, and frequency of deranged laboratory findings, we hope to improve our ability to predict and manage cases in a timely and appropriate manner. The mean age of the study participants was 7.9±3.7 years, ranging from 4-7 years. The male-female ratio was 1.2:1. Similar results were reported by the study done by [19]…….. found mean age was 6.9±3.3 years, the male: female ratio was 1.2:1, and that found common age group of 5-10 years, the female ratio was 1.3:1. In this study, more than half (52.0%) of patients had DSS during admission followed by 17.3% in DHF and 10.7% in EDS. Sixteen percent patients of with DSS progressed to DHF and 4.0% patients of with DHF progressed to EDS after admission and during the hospital stay. 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 was needed in 98.7% of the patients and the average ICU stay was ≤3 days in 80.0% of patients. [20]

However Mishra et al reported 63.9% of patients were admitted to the ICU for 3–6 days.[21] Fever was the most common clinical feature and was present in 97.3% of patients which is comparable to the earlier observations whereas reported fever in 94.6% [22]…… reported fever in 93% of patients [23] reported fever in 96.8% of patients. Abdominal pain and vomiting were the second most common clinical feature and was present in 77.3% of patients which is like other reports. [24] reported abdominal pain as the second most clinical feature followed by vomiting. [25] 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 and clinical accumulation of fluid were the most common warning sign in SD. In this study, we found rash in 28 cases (18.7%) and Shock in 94 cases (62.7%) which were prominent features of SD. [26] found shock in 70.8% of patients.

The most common bleeding manifestation was hematemesis and melena in 24 cases (16.0%) which was supported by the study done by Srivastava et al reported 90%, and Ahmed reported 61% had GIT hemorrhages.[27] Pleural effusion was the most common physical finding seen in 70 cases (46.6%) followed by ascites in 52 cases (34.7%) then 32 cases (21.3%) had hepatomegaly. But other studies by [28] where hepatomegaly was the most common physical finding. Normal leukocyte count was present in 63.54% of the cases, while leucopenia was seen in 42 cases (28%) which was consistent with other studies. But [29] showed leukopenia was significantly related to severe dengue cases which was against our result. It was shown that among the liver enzymes, AST was elevated in a larger proportion in 90 cases (60%), this finding was similar to the study done by where they found AST was elevated in 47.42% of patients when compared to alanine aminotransferase (ALT) which was 30.92%. Low albumin was found in 118 cases (78.7%), which was almost similar to the value (72.8%) obtained by [30], but much higher than the value (33%) obtained by [31, 32].

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% followed by left-sided effusion in 6.7% of cases which was consistent with the study done by right-sided effusion (15.46%) was most commonly seen followed by bilateral effusion (6.18%). In this study hyponatremia was found in 70 cases (46.7%) followed by hypokalaemia in 28 cases (18.7%) were most common electrolyte abnormalities which was consistent with the study where hyponatremia was found in 45.33% and hypokalaemia in 10.60% of cases.[33] also reported that hyponatremia and hypokalaemia were common electrolyte abnormalities. Serum electrolyte 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 as well as mortality.[34] showed coagulopathy as a significant risk factor for mortality. Raised D-dimer and low fibrinogen was found in 70.7% and 56.0% of the cases respectively which are an indicator of dengue severity like DHF whereas [35] showed significantly higher D-dimer levels in DHF patients compared with DF patients with sensitivity of D-dimer in predicting DHF of 90 %. DD was also found to be positively correlated with dengue severity in all stages of the disease namely febrile, toxic, and convalescent (P-value <0.05).

Consistency with this study raised D-dimer and low fibrinogen was found in 70.7% and 56.0% of patients respectively. In our study, we found 52 cases (34.7%) had prolonged PT, 56 cases (37.3%) had prolonged aPTT which was higher than the [36] where 20.9% had prolonged PT and 33.3% had prolonged aPTT. The common blood group in this study was B+ which was in 37.3% of patients. A similar result was found in the study done by [37] found common blood group O positive 42.8%.[38] found common blood group was O positive and the B group is more prevalent in children which was similar to our study. In this study, 25.3% of patients were obese, and 17.3% of patients were overweight. Almost all obese and overweight patients presented with DSS. [38] Reported that the prevalence of DHF with shock is fifty percent and DHF without shock was 50%. The prevalence of obesity was 40.9% and the severity of DHF was significantly correlated with a P-value of 0.004. In our study majority of the cases (94.7%) were recovered. We observed 5.3% of death in severe dengue in our study. Among 4 patients who died three of them were obese, developing DIC with multi-organ failure. The rest had severe acute asthma with sepsis with intractable shock. However, a recently published article by in Dhaka city

showed case fatality rate was 12.1% among severe dengue.

Limitations

This single-center study on dengue fever exclusively focused on hospitalized cases, with no control group included. The diagnosis was established through either dengue NS1 antigen testing or dengue serology and PCR. However, the study did not involve viral isolation or serotype identification.

CONCLUSION

Severe dengue fever is a dreaded illness among children. However, timely diagnosis and management can significantly reduce the case fatality rate despite its varied presentations and features. Our study comprehensively outlines the typical and atypical symptoms, severity grading, investigations, and management protocols based on the latest national guidelines. Severe cases often exhibit dominant features such as abdominal pain, vomiting, shock, ascites, and pleural effusion. Significant laboratory findings include raised AST and D-dimer, low fibrinogen and albumin levels, and hyponatremia. Early detection and efficient management are crucial in mitigating the severity of the disease.

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