Clinical, Hematological and Biochemical Profile of Dengue Syndromesin Children

Abstract

Background: Dengue is a viral disease transmitted by mosquito bites with arising global incidence, more commonly afflicting children in endemic countries such as Bangladesh. Among the severe forms, such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), there are hematological and biochemical complications. This study aims to evaluate the clinical, hematological and biochemical predictor of severity in pediatric dengue syndromes with the intention of improved clinical management.

Methods: A cross sectional analytical study conducted at the Department of Pediatrics, Dhaka Medical College Hospital from April 2019 to March 2020. A total of 350 hospitalized children aged 1 month to 12 years with confirmed dengue positive were included in this study. Descriptive statistics were performed on clinical symptoms, hematological parameters and biochemical markers in order to test corresponding standard significance tests.

Results: The most common symptoms were high grade fever (93.14%); vomiting (78.86%); abdominal pain (43.14%). 14.85% of DSS cases had severe thrombocytopenia (<20,000 cells/mm^3). 13.86 % of DSS cases had elevated hematocrit (>45 %). In severe cases there were biochemical derangements including high SGPT (59.76% in DHF) and prolonged PT (>16 seconds). In DSS 35.15% were hypoproalbuminemic (< 3.0 gm/dl). Expanded dengue syndrome was characterized by hypocalcemia (62.5%) and elevated serum creatinine (25%).

Conclusion: The clinical and laboratory markers highlighted here for early detection of severe dengue in children will help in early intervention to reduce morbidity and mortality.

Keywords: Dengue, Hematological abnormalities, Biochemical derangements, Pediatric syndromes.

Introduction

Dengue fever is one of the most rapidly spreading mosquito-borne viral infections worldwide. Dengue virus belongs to the Flavivirus genus which includes 4 known types of serotypes (DENV 1-4). Aedes aegypti and Aedes albopictus mosquitoes are primarily vectors of transmission and can be found in tropical and subtropical climates [1,2]. Despite year after year of a global burden of nearly 390 million dengue infections, only about a quarter become clinically apparent. Severe forms of the disease are particularly common in children and make substantialcontributions to morbidity and mortality caused by dengue [3,4].

A dramatic rise in the number of cases has occurred in Bangladesh and the country has seen repeated dengue epidemics. The outbreaks in 2000 and 2019 significantly increased pediatric cases, including severe forms such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) and demand urgent attention [5,6]. In studies done in Dhaka and other urban areas, it is found that children constitute a large proportion of hospital admissions during outbreaks with changes in clinical and hematological profiles [7]. These presenting symptoms include high grade fever, vomiting, abdominal pain, bleeding

tendency and skin rash that are complicated in severe cases by plasma leakage, thrombocytopenia and organ dysfunction [8, 9].

Diagnosis and prognosis of dengue simply depend on hematological abnormalities. Hallmark features of disease severity are thrombocytopenia, leukopenia, and elevated hematocrits. Severe dengue is associated with elevated liver enzymes (SGPT and SGOT) and prolonged coagulation parameters (PT and APTT), and has been shown to be useful in early identification of complications [10,11]. The two serological tests (NS1 antigen and dengue specific antibodies (IgM and IgG) are used to confirm the diagnosis, along with these parameters.

Despite management guidelines, early detection and successful treatment are still difficult, especially in pediatric populations [13]. Resource constraints are common to healthcare facilities in Bangladesh, complicating management of severe dengue cases. This reinforces the requirement for comprehensive clinical, hematological and biochemical profiles that are unique to patients and should be used to improve diagnostic accuracy and therapeutic outcomes [14].

This study was carried out for the purpose of analysis of hematological abnormalities and biochemical changes associated with clinical features in children with different dengue syndromes in a tertiary care hospital of Dhaka. The study identifies significant predictors of severity to bridge knowledge gaps and provide guidance for targeted interventions for pediatric patients. These findings are expected to help guide clinical decision making for dengue in resource limited settings and reduce morbidity and mortality.

Objectives

The objective of this study was to find out the clinical and hematological profile of Dengue syndrome in Children.

Materials&Method

A cross-sectional analytical study was carried out in the Pediatrics Department of Dhaka Medical College and Hospital (DMCH) from April 2019 to March 2020. The study included 350 hospitalized children, ranging from one month to 12 years old of both sex. These patients exhibited clinical signs suggestive of dengue and tested positive for NS1 antigen and/or dengue antibodies (IgM, IgG, or both) through serology. The participants were categorized into five groups: undifferentiated fever (UDF), dengue fever (DF), dengue hemorrhagic fever (DHF), dengue shock syndrome (DSS) and expanded dengue syndrome (EDS) following the WHO dengue classification criteria..

Inclusion Criteria:

1. Children who admitted with fever and clinical features of dengue with positive NS1 antigen test and/ or dengue antibody serology IgM or IgG or both
2. Children aged from 01 month to 12 years

Exclusion criteria:

1. Patients with other comorbid conditions that can alter patient's biochemical and haematological parameters like typhoid fever, malaria, malignancy congenital heart disease, chronic liver disease.

Study procedures: This analytical, cross-sectional study was conducted in Department of Pediatrics, DMCH for 12 months. Patients admitted with fever and clinical manifestations of dengue with positive NS1 antigen test and/or dengue antibody serology IgM or IgG or both were included. NS1 was done in patients presenting with fever for 3 days or less and Dengue IgM and IgG for those with fever for more than 5 days.

History and physical examination was conducted. History was included age, sex, fever details, headache, myalgia, arthralgia, skin rash, anorexia, nausea/vomiting, abdominal pain, urine output, convulsion and others. Physical examination was included pallor, respiratory rate, heart rate, temperature, blood pressure, Capillary Refill Time (CRT), tourniquet test, skin condition, hepatomegaly, ascites, pleural effusion, bleeding manifestations. Complete blood count was done in all patients. SGPT, SGOT, PT, APTT levels was done in severe dengue (DHF and DSS). Serum albumin was done as an evidence of plasma leakage. Information was collected by using a semi-structured questionnaire. Resuscitation of emergency signs and symptoms was done according to the 'National Guideline for management of dengue syndromes.

Statistical analysis of data: The data were analyzed using SPSS version 21. Descriptive statistics were used to summarize the clinical, hematological, and biochemical parameters. Categorical variables were compared using the chi-squared test. Continuous variables were expressed as mean ± standard deviation (SD) and were analyzed using Student's t-test. Statistical significance was set at $P < 0.05$.

Results

Table 1: Baseline characteristics of the study subjects (n=350)

Characteristics		No. of patients	Percentage (%)
Age group	1 month-1 year	10	2.86
	1-4 year	60	17.14
	4-9 year	126	36.00
	9-12 year	154	44.00
Gender	Male	207	59.14
	Female	143	40.86
Types of Dengue syndrome	UDF	18	5.14
	DF	40	11.43
	DHF	82	23.43
	DSS	202	57.71
	EDS	8	2.29

This table presents the age and gender distribution of the study participants. The majority of the children were aged 9–12 years (44%), and males constituted 59.14% of the sample. Among the different types of dengue syndrome, Dengue Shock Syndrome (DSS) was the most common presentation, affecting 57.71% of patients. Dengue Hemorrhagic Fever (DHF) was observed in 23.43%, while Dengue Fever (DF) accounted for 11.43%. Undifferentiated Fever (UDF) was seen in 5.14% and Expanded Dengue Syndrome (EDS) was the least common, affecting 2.29%.

Table 2: Distribution of symptoms in children with Dengue Syndrome (N=350)

Parameter	No. of patients	Percentage (%)

Fever	Low grade	24	6.86
	High grade	326	93.14
Duration	<5 days	168	48.00
	≥5 days	182	52.00
Skin rash		33	9.43
Maculopapular		27	7.71
Rubelliform		3	0.86
Flushing		5	1.43
Bleeding		120	34.29
Vomiting		276	78.86
Abdominal Pain		151	43.14
Convulsion		3	0.86

The table outlines the clinical symptoms observed. High-grade fever was the most common symptom (93.14%), followed by vomiting (78.86%) and abdominal pain (43.14%). Bleeding manifestations were seen in 34.29% of cases, and only 9.43% exhibited skin rashes.

Table 3: Dengue serology in subjects with dengue syndromes (N=350)

Parameters	UDF (n=18)	DF (n=40)	DHF (n=82)	DSS (n=202)	EDS (n=8)	Total (n=350)
NSI	16 (88.89)	36 (90)	70 (85.37)	174 (86.14)	6 (75)	302 (86.29)
IgM only	2 (11.11)	3 (7.50)	8 (9.76)	18 (8.91)	2 (25)	33 (9.43)
IgG only	0 (0)	0 (0)	1 (1.22)	8 (3.96)	0 (0)	9 (2.57)
IgM+IgG	0 (0)	1 (2.50)	3 (366)	2 (0.99)	0 (0)	6 (1.71)

This table shows serological findings across different dengue syndromes. NS1 antigen was positive in 86.29% of cases, while IgM antibodies were detected in 9.43%, and IgG antibodies in 2.57%. Dual IgM and IgG positivity were rare (1.71%).

Table 4: Haemoglobin (Hb) and haematocrit (HCT) % among groups (N=350)

Parameters		UDF (n=18)	DF (n=40)	DHF (n=82)	DSS (n=202)	EDS (n=8)	p-value
Hb (gm/dl)	<10	4 (22.22)	2 (5.0)	12 (14.63)	24 (11.88)	2 (25.00)	0.03
	10-15	14 (77.78)	38 (95.00)	64 (78.05)	150 (74.26)	5 (62.50)	
	>15	0 (0)	0 (0)	6 (7.32)	28 (13.86)	1 (12.50)	
HCT (%)	<25	0 (0)	0 (0)	6 (7.32)	6 (2.97)	0 (0)	0.12
	25-35	13 (72.22)	14 (35.0)	27 (32.93)	61 (30.20)	4 (50.0)	
	35-45	5 (27.78)	26 (65.0)	42 (51.22)	107 (52.97)	4 (50.0)	
	>45	0 (0)	0 (0)	7 (8.54)	28 (13.86)	0 (0)	

This table examines Hb and HCT levels for different dengue syndromes. Majority of children had Hb levels between 10 and 15 gm/dl. Severe cases including DSS (11.88%) were more frequent in anemia (Hb <10 gm/dl). In 13.86% of DSS cases and 8.54% of DHF case, hematocrit levels were above 45%, a sign of plasma leakage.

Table 5: TLC (cells/mm³), neutrophil (%) and lymphocyte (%) among groups (N=350)

Parameters		UDF (n=18)	DF (n=40)	DHF (n=82)	DSS (n=202)	EDS (n=8)	p-value
TLC (cells/mm3)	<4000	0 (0)	11 (27.50)	16 (19.51)	44 (21.78)	2 (25.0)	0.06
	4000-11000	16 (88.89)	26 (65.0)	57 (69.51)	134 (66.34)	2 (25.0)	
	>11000	2 (11.11)	3 (7.50)	9 (10.98)	24 (11.88)	4 (50.0)	
Neutrophil (%)	<40	2 (11.11)	16 (40.0)	34 (41.46)	81 (40.10)	1 (12.5)	0.11
	40-60	12 (66.67)	12 (30.0)	32 (39.02)	78 (38.61)	4 (50.0)	
	>60	4 (22.22)	12 (30.0)	16 (19.51)	43 (21.29)	3 (37.5)	
Lymphocyte (%)	<20	3 (16.67)	6 (15.0)	4 (4.88)	17 (8.42)	1 (12.5)	0.46
	20-40	4 (22.22)	11 (27.50)	21 (25.61)	56 (27.72)	4 (50.0)	
	>40	11 (61.11)	23 (57.50)	57 (69.51)	129 (63.86)	3 (37.5)	

This table focuses on total leukocyte count (TLC), neutrophil, and lymphocyte percentages, highlighting hematological abnormalities. Among DSS and DHF we commonly have leukopenia (<4,000 cells/mm³) (21.78). All groups had lymphocytosis (> 40%) and neutrophils were variable, with neutropenia more common in severe cases; DSS cases were most common (63.86%).

Table 6: Total platelet count /TPC (cells/mm³) of the subjects among groups (N=350)

Parameters	UDF (n=18)	DF (n=40)	DHF (n=82)	DSS (n=202)	EDS (n=8)	p-value
<20000	0 (0)	0 (0)	9 (10.98)	30 (14.85)	1 (12.5)	<0.001
20000-50000	0 (0)	6 (15.0)	29 (35.37)	67 (33.17)	0 (0)	
50000-100000	0 (0)	18 (45.0)	24 (29.27)	58 (28.71)	0 (0)	
100000-150000	0 (0)	16 (40.0)	14 (17.07)	25 (12.38)	2 (25.0)	
150000-450000	16 (90.0)	0 (0)	6 (7.32)	22 (10.89)	5 (62.5)	
>450000	2 (10.0)	0 (0)	0 (0)	0 (0)	0 (0)	

This table expands on platelet counts in dengue syndromes as a critically important parameter to assess disease severity. We found severe thrombocytopenia (<20,000 cells/mm³) in 14.85% of DSS cases and 10.98% of DHF cases. The risk of bleeding complications was highlighted in most DHF and DSS patients with platelet counts between 20,000 and 100,000 cells/mm³.

Table 7: SGPT and SGOT level (U/L) among study groups (N=350)

Parameters	UDF (n=18)	DF (n=40)	DHF (n=82)	DSS (n=202)	EDS (n=8)	p-value

SGPT (U/L)	≤45 Normal	17 (94.44)	33 (82.50)	23 (28.05)	89 (44.06)	3 (38.0)	<0.001
	45-200	1 (5.56)	7 (17.50)	49 (59.76)	107 (52.97)	1 (12.0)	
	200-1000	0 (0)	0 (0)	10 (12.20)	6 (2.97)	0 (00	
	>1000	0 (0)	0 (0)	0 (0)	0 (0)	4 (50.0)	
SGOT (U/L)	≤60 Normal	17 (94.44)	34 (85.0)	20 (24.39)	75 (37.13)	4 (50.0)	<0.001
	60-200	1 (5.56)	6 (15.0)	43 (52.44)	105 (51.98)	0 (0)	
	200-1000	0 (0)	0 (0)	19 (23.17)	22 (10.89)	0 (0)	
	>1000	0 (0)	0 (0)	0 (0)	0 (0)	4 (50.0)	

P-value obtain from chi-square test

This table summarizes liver function abnormalities in dengue syndromes. In DHF, 59.76% were found to have elevated SGPT levels (45–200 U/L) suggestive of liver involvement and in DSS cases 52.97% had elevated SGPT levels (45–200 U/L). Similarly, 52.44% of DHF and 51.98% of DSS cases showed elevated SGOT levels (60–200 U/l). Severe elevations (RQ > 200 U/L) were rare but had a strong implication toward severe dengue.

Table 8: PT (sec), APTT (sec) and S. Albumin (gm/dl) level among study groups (N=350)

Parameters		**UDF (n=18)**	**DF (n=40)**	**DHF (n=82)**	**DSS (n=202)**	**EDS (n=8)**	**p-value**
PT (sec)	>16	0 (0)	0 (0)	24 (29.27)	16 (7.92)	4 (50.0)	<0.001
	≤16	18 (100.0)	40 (100.0)	58 (70.73)	186 (92.08)	4 (50.0)	
APTT (sec)	>36	0 (0)	1 (2.50)	11 (13.41)	26 (12.87)	.3 (37.0)	<0.001
	≤36	18 (100.0)	39 (97.50)	71 (86.59)	176 (87.13)	5 (63.0)	
Albumin (gm/dl)	<3.0	0 (0)	0 (0)	16 (19.51)	71 (35.15)	1 (12.0)	<0.001
	≥3.0	18 (100.0)	40 (100.0)	66 (80.49)	131 (64.85)	7 (88.0)	

This table evaluates coagulation and plasma leakage markers. In severe cases, Prolonged PT (> 16 seconds) and APTT (> 36 seconds) were common and observed in patients with DHF 29.27% and 13.41%, respectively. A prevalence of 35.15% for hypoalbuminemia (<3.0 gm/dl), a marker for plasma leakage, noted in DSS cases was correlative of disease severity.

Table 9: Random blood sugar, s. calcium and s. creatinine of EDS subjects (n=8)

Parameters	**Frequency (%)**
Random blood sugar (m mol/l)	
Low (<3.3)	2 (25.0)
Mean±SD	4.2±0.6
S. Calcium (mg/dl)	
Low (<8.8)	5 62.5
Mean±SD	8.10±0.8
S. Creatinine	

Raised (≥1.0)	2 (25.0)
Mean±SD	0.97±0.6

This table shows the biochemical abnormalities for ED's cases. The most common abnormality was hypocalcemia (< 8.8 mg/dl) in 62.5 %, and low random blood sugar (< 3.3 mmol/L) in 25 % suggesting metabolic derangement. However, 25% of cases had elevated serum creatinine (≥1.0 mg/dl) as a result of renal involvement.

Discussion

This study finds significant clinical, hematological and biochemical profiles of pediatric dengue syndromes consistent with previous literatures but uniquely specific to the Bangladeshi pediatric population.

Among the most prevalent symptoms in this group was high grade fever, vomiting, and abdominal pain, as was observed by Alam et al. in their pediatric dengue patients in Bangladesh [2]. The frequency of bleeding manifestations in this study (34.29%) also agrees with the findings of Majeed et al. in the tertiary care, where about one third of cases were having severe bleeding [12]. However, the low prevalence of skin rashes (9.43%) was contrasted by the observations by Shekar [et al. of higher rates (20%) in Indian pediatric populations [8]. The variation could be due to geographical or genetic differences in how dengue presents.

This study was characterized by hematological abnormalities especially thrombocytopenia and leukopenia. As seen in Meena et al., severe dengue patients in India [13], we found 14.85% severe thrombocytopenia (90,000 cells/ mm^3). The agreement also found with Kotwal et al. who highlighted the importance of Leukopenia as a key diagnostic criterion for severe dengue [14], as this was observed in 21.78% of cases here. Furthermore, hematocrit levels above baseline (>45%) indicative of plasma leakage were found in 13.86% of DSS cases, which again confirmed the work of Tewari et al. that hematocrit elevation strongly correlates with disease severity [15].

In this study, biochemical changes were significant with elevated SGPT and SGOT levels. A SGPT elevation of >45–200 U/L was observed in 59.76% of DHF cases, similar to that seen in Tahlan et al. in their study of >60% of severe dengue cases [16]. Long PT and APTT were also more frequent in severe dengue cases, indicative of coagulopathy as a significant complication of dengue. As noted by Patel et al., in case of severe disease prolonged coagulation times were observed [10].

Severe pediatric dengue cases in these circumstances also have rates of hypoalbuminemia (plasma leakage) equal to 35.15%, similar to 27% reported in Shah et al. in Nepal severe cases in severe pediatric dengue cases in Nepal [17]. This further confirms hypoalbuminemia as a key prognostic indicator for dengue severity.

The serological profile showed high NS1 antigen positivity (86.29%), suggesting its advantage as an early marker of the disease, particularly during the first week.Similarly, Joshi et al. highlighted the reliability of NS1 antigen in early dengue diagnosis, especially for resource-limited settings [6]. This study differs from this however, as IgM and IgG antibody positivity was less frequent in this study, similar to Oza et al. where early phase cases predominantly showed NS1 positivity [18].

However, metabolic derangements, including hypocalcemia (62.5%) and elevated creatinine (25%) in ED's cases, suggest that severe dengue has other complications. These findings are consistent with the findings of Mutsuddy et al., who found renal and metabolic abnormalities as important concerns emerging

in expanded dengue syndromes in Bangladesh [4]. This was corroborated by the reported low random blood sugar (less than 33 mmol/L) in 25% of EDS cases, as described in Hamed et al., suggesting metabolic obstacles brought about by severe dengue [9].

Our findings also compared to national guideline for dengue management in Bangladesh (Islam et al.) and significant overlap was found in key markers of disease severity including thrombocytopenia, hematocrit elevation and hypoalbuminemia [11]. Nevertheless, the high incidence of vomiting and abdominal pain in this study emphasizes that gastrointestinal symptoms should receive greater weight in future versions of the guidelines in order to timely recognize and manage pediatric dengue.

Conclusion

This study presents valuable clinical, hematological and biochemical profiles of pediatric dengue syndromes in Bangladesh. These findings reinforce the critical importance of recognizing hematological and biochemical derangements early in severe dengue to prevent complications and improve outcomes in children.

Limitations and recommendations

This was a single center study and the findings may not reflect the whole population of the pediatric population of Bangladesh. In addition, the cross-sectional design does not allow us to establish causality between observed biochemical changes and disease progression. These findings were validated through future multicenter, longitudinal studies to validate them and assess their broader applicability.

Ethical Approval and consent:

Ethical approval was obtained from the DMCH ethical review board. Informed written consent from the parents/attendant was taken prior to include the child in the study after detailing the aims & objectives of the study and its implication on the child and overall in pediatric science in Bangladesh and in the world. All data were handled confidentially. Only the investigator, regulatory authority and ethical review committee had access to such information. The identity of the patient was not disclosed while analyzing or publishing the results of this study. For safeguarding confidentiality and protecting anonymity, each of the patients had given a special ID no. which was followed in each and every step of data collection, editing, storage and analysis.

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