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Original Research Article

Dengue and severe dengue fever: comparison of clinical characteristics, haematological and biochemical parameters in a tertiary care hospital

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ABSTRACT

Background: Dengue is a mosquito-borne viral disease worldwide. The number of new cases and death in Bangladesh increased in current years. The aim of the study was to detect the difference between demographic data, warning signs, comorbidity, treatment pattern, and laboratory investigations in two different types of dengue fever during the pick season.

Methods: This retrospective observational study was done in Holy Family Red Crescent Medical College from May to October 2021 from records of hospital on a total of 113 dengue NS1, IgG and IgM positive patients. The classical dengue fever (CDF) group consists of 76 and dengue hemorrhagic fever (DHF) group consists of 37 patients. Socio-demographic data, co-morbidity (DM, HTN, Bronchial Asthma, COVID-19), 'warning sign' (abdominal tenderness, mucosal bleeding, lethargy, restlessness, persistent vomiting, clinical fluid accumulation, liver enlargement >2cm, increase HCT, decrease Platelet), treatment pattern, and laboratory findings were assembled, analyzed and compared between two groups.

Results: Out of 113 patients, the majority were male. The mean age of patients was (26.0±15.8 and 27.7±17.2) in CDF and DHF. The mean duration of hospital stay was slightly longer in DHF (6.78±2.1 days) compared to CDF patients (6.13±1.45 days). The co-morbidities were similar between groups. Among warning signs, only mucosal bleeding was significantly more in DHF (37.8%) than in CDF patients (7.9%) (p <0.001). Similarly, decreased HCT and clinical fluid accumulation were significantly higher in the DHF group (p <0.001 and p=0.024).

Conclusions: The frequency of CDF was higher than DHF, but the 'warning sign' and significant thrombocytopenia and leucopenia in DHF reflect the progression to dengue shock syndrome.

Keywords: Dengue, Warning sign, Antibiotics, Corticosteroid, Haematological

INTRODUCTION

For past three decades, dengue has unrelenting to a stance foremost the public health problem globally. Universally,

there are nearly 100 million infections reported each year with up to 2% ensuing in a deadly outcome¹. These outbursts untiringly defy provincial health systems and the frugality, predominantly in emerging countries where they

are more prevailing. The financial sway of dengue in India in 2006 was appraised to be USD 27 million². Dengue fever and dengue hemorrhagic fever are common in Southeast Asia, Thailand, Vietnam, Singapore, and Malaysia, and in recent times in Bangladesh³.

Dengue fever is a mosquito-borne infection started with the sudden onset of high fever. Dengue infection may be with symptoms and without symptoms. Symptomatic dengue infection is grouped into classical dengue fever (CDF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS). CDF is known as saddleback or biphasic, break-bone fever, associated with muscle pain, headache, retro-orbital pain, and a rash.^{4,5} The disease proceeds to a critical phase as fever resolves.⁶

Plasma leakage is the marked clinical feature of dengue hemorrhagic fever and well-timed and precise diagnosis and controlling of plasma leakage phase is critical for better patient outcome.⁷ Successions of biochemical and hematological changes occur during the progress of the illness. They could be used to detect the complications early and introduce effective management approaches thus reducing morbidity and mortality. Hematological and biochemical parameters like hematocrit, albumin concentration, platelet count and aspartate aminotransferase ratio in combination is shown to be effective in identifying patients with plasma leakage in severe dengue in Bangladesh, the first surge of dengue fever was observed in 1964 in Dhaka and the first epidemic of DHF was observed in mid of 2000, total of 5,551 dengue diseased cases were reported in Dhaka, Chittagong, and Khulna cities (adults were more frequent). The case fatality rate was documented by 1.7% with 93 deaths reported⁸. Directorate General of Health Service (DGHS) of Bangladesh reported that 1,01,354 confirmed the case. and 164 deaths in the year 2019.⁹ No specific antiviral drugs are available to treat dengue fever. Treatment depends on the clinical features of the individual patient and proper fluid balance is the key module of the treatment.¹⁰

National guideline of Bangladesh recommended that patients have “no warning signs” managed at home with daily follow-up and oral rehydration therapy. Patients who have high risk co morbidities, have “warning signs”, or cannot accomplish regular follow-up should be admitted to the hospital. After admission, the amount of fluid management is titrated to unwavering vital signs and normalization of hematocrit level.¹¹ Other than acetaminophen, NSAIDs like ibuprofen and aspirin are avoided to decrease the risk of bleeding. Packed red blood cells or whole blood are recommended, rather than platelets and fresh frozen plasma.¹⁰ Corticosteroids also have a controversial effect on dengue fever.¹² Hepatic involvement of varying severity is also increasingly recognized related to dengue infection.^{13,14} Derangement of liver function tests characterized by mildly raised serum total bilirubin, increased alanine transaminase (ALT) and aspartate transaminase (AST), and decreased serum

albumin is commonly seen in Dengue infection and can be useful as prognostic markers.¹⁵⁻¹⁷ During the plasma leakage phase of the illness, calcium, albumin and cholesterol levels also reduce in the serum.¹⁸ Despite this management, dengue fever has become a grave condition nowadays. Many people die and many are in danger, especially in Dhaka city. The current study is aimed to observe the variation in comorbidities, warning signs, treatment pattern, and change in their biomarker in CDF and DHF affected infection.

METHODS

This retro-prospective observational study was held in a 720-bed non-government Holy Family Red Crescent Medical College Hospital (HFRCMCH), Dhaka, Bangladesh from May to October 2021. The study was approved by the designated hospital authority and the institutional ethics review board (IERB). All dengue NS1, IgG and IgM positive patients of 2 to 60 years of age range, admitted with a ‘warning sign’ (clinical observations need hospitalization for close monitoring) / high-risk condition (host factors donates to more severe condition of the disease and its complications) in hospital in the study period were included. Patients diagnosed with other fever and unavailability of all data were excluded from the study. 113 cases were conveniently selected as the study population. 113 patients were divided into two groups, 76 patients in the classical dengue fever (CDF) group, and 37 patients in the dengue hemorrhagic fever (DHF) group. Demographic data (age, gender, length of hospital stay), ‘warning signs based on clinical sign (abdominal tenderness, mucosal bleeding, lethargy, restless ness, persistent vomiting) and clinical examination and lab investigation (clinical fluid accumulation, liver enlargement >2cm, increase HCT, decrease platelet), high-risk co-morbidity (DM, HTN, Bronchial Ashma, COVID-19), treatment pattern, and lab investigation report along with patient personal record file were collected from hospital record room. All data are written in custom-made proforma. Statistical analysis was done using SPSS version 21.0 and all p values were two-tailed, with p <0.05 considered statistically significant.

Aim and objectives

Therefore, this prospective follow-up study was designed, to study the pattern of change of biochemical and hematological parameters in CDF and DHF among Bangladeshi population, and to assess their efficacy as early predictors of entry into critical or plasma leaking phase.

RESULTS

All serologically positive (NS1, IgG and IgM) dengue patients were included in the study.

Table 1 shows the comparison of demographic profile, high-risk co-morbidities, and warning signs between

patients with CDF (n=76) and DHF (n=37). The mean age of patients was comparable between the two groups (26.0 ± 15.8 years vs. 27.7±17.2 years; p=0.689), with a male predominance observed in both groups, though the difference was not statistically significant (p=0.513). The mean duration of hospital stay was slightly longer in DHF patients (6.78±2.1 days) compared to classical dengue patients (6.13±1.45 days), but this difference did not reach statistical significance (p=0.061). The distribution of high-risk co-morbidities such as hypertension, diabetes mellitus, bronchial asthma, COVID-19, and other conditions was

similar between the groups (p>0.05 for all). Among warning signs, mucosal bleeding was significantly more frequent in DHF patients (37.8%) than in classical dengue patients (7.9%) (p< 0.001). Similarly, decreased haematocrit (HCT) and clinical fluid accumulation were significantly higher in the dengue haemorrhagic fever group (p<0.001 and p=0.024, respectively). Other clinical warning signs, including restlessness, abdominal tenderness, lethargy, persistent vomiting, increased platelet count, and liver enlargement (>2 cm), did not show statistically significant differences between the two groups.

Table 1: Comparison of demographic characteristics, co-morbidities, and warning signs between classical dengue and dengue haemorrhagic fever patients (n=113).

Characteristics	Classical dengue (n=76)	Dengue hemorrhagic fever (n=37)	Statistical significance test	
Age (mean±SD)	26 ±15.8	27.7± 17.2	0.689	
Gender	Male	21(56.8%)	0.513	
	Female	16(43.2%)		
Length of hospital stay(days) mean±SD	6.13±1.45	6.78±2.1	0.061	
High risk co-morbidities				
Hypertension	16(21.1%)	5(13.5%)	0.334	
Diabetes mellitus	6(7.9%)	3(8.1%)	0.969	
Bronchial asthma	2(2.6%)	0(0.0%)	0.319	
Covid-19	0(0.0%)	2(5.4%)	0.105	
Others	7(9.2%)	4(10.8%)	0.788	
Presence of 'warning sign'-no/total no. (%)				
By clinical sign	Mucosal bleeding	6 (7.9%)	14 (37.8%)	<0.001**
	Restlessness	5 (6.6%)	4 (10.8%)	0.472
	Abdominal tenderness	6 (7.9%)	5 (13.5%)	0.500
	Lethargy	13 (17.1%)	7 (18.9%)	0.798
	Persistent vomiting	38 (50.0%)	15 (40.5%)	0.423
By clinical examination and lab findings	Increased platelet	52 (68.4%)	23 (62.2%)	0.530
	Decreased HCT	75 (98.7%)	24 (64.9%)	<0.001**
	Liver enlargement >2 cm	13 (17.1%)	11 (29.7%)	0.145
	Clinical fluid accumulation	2 (2.6%)	5 (13.5%)	0.024*

*Significant at p<0.05, **highly significant at p<0.001.

Table 2: Comparison of treatment modalities among patients with classical dengue fever and dengue haemorrhagic fever (n=113).

Drugs	Classical dengue fever (n=76)	Dengue hemorrhagic fever (n=37)	P value
Fresh frozen plasma transfusion	15 (19.7%)	13 (35.1%)	0.104
Antibiotic			
Cephalosporins	24 (31.6%)	12 (32.4%)	1.000
Fluroquinolones	21 (27.6%)	6 (16.2%)	0.242
Meropenem	1 (1.3%)	2 (5.4%)	0.249
Steroids	33 (43.4%)	18 (48.6%)	0.688
Plasma+steroid	7 (9.2%)	4 (10.8%)	0.748
Tranexamic acid	16 (21.1%)	9 (24.3%)	0.810

Table 2 shows that most of the patients received intravenous infusion during their hospital stay. Among them (75.61%, 87.45%) received 1000 ml/day in both groups. 10 patients did not get any intravenous infusion in CDF group. Total 15 (19.7%) patients out of 113 received fresh frozen plasma which was higher than CDF

13(35.1%). The difference was not significant (p=0.104). Among the antibiotics cephalosporins was the most commonly prescribed (31.6%, 32.4%), in both groups. Corticosteroids were used in higher percentage in DHF (48.6%) compared to CDF (43.4%). Tranexamic acid was also largely used in DHF (24.3%) than CDF (21.1%). The

use of antibiotics, plasma plus steroid therapy, and tranexamic acid was comparable between the two groups, with no statistically significant differences observed in treatment patterns ($p > 0.05$ for all).

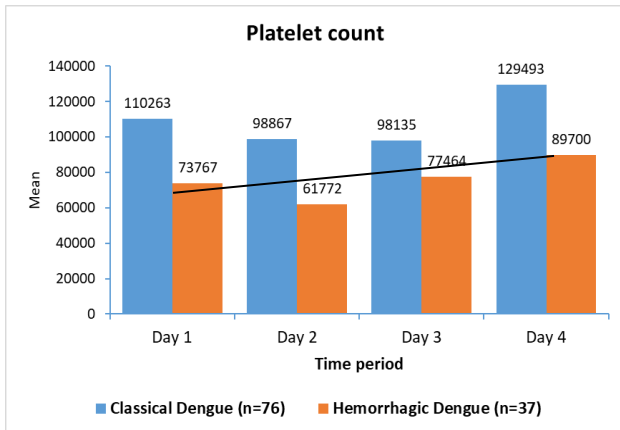


Figure 1: Comparison of mean platelet count between classical and haemorrhagic dengue patients over four days of hospitalization.

The comparison of serial hematological parameters between classical and hemorrhagic dengue patients were done over four consecutive days of hospitalization. Hemoglobin (range 12 to 13 gm/dl) and hematocrit levels (range 36 to 38) remained comparable between the two groups throughout the study period. Total white blood cell counts also showed wide variability in both groups but did not differ significantly across the four days.

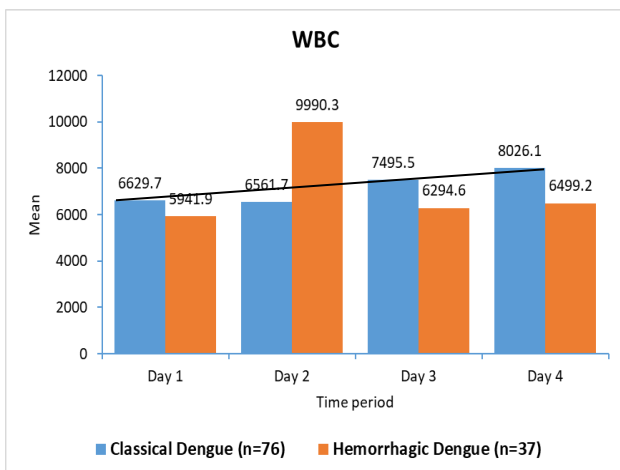


Figure 2: Comparison of mean WBC count between classical and haemorrhagic dengue patients over four days of hospitalization.

In contrast, platelet counts were consistently lower in hemorrhagic dengue patients compared to classical dengue. This difference was statistically significant on day 1 ($p = 0.012$), day 2 ($p < 0.001$), and Day 4 ($p = 0.002$), while the difference on Day 3 approached but did not reach statistical significance ($p = 0.073$) in an unpaired t-test. Whereas, WBC count was not significant. (Figure 1 and

2). Other supportive investigations like SGPT, serum creatinine ($p = 0.026$), electrolytes Na ($p = 0.041$), K ($p = 0.001$), Cl were also done. Among radiological findings chest X-Ray and USG showed higher percentage of fluid accumulation in DHF compared to CDF. Only mild ascites was statistically significant ($p < 0.005$) among groups.

DISCUSSION

Dengue fever, also well-known as breakbone fever for the extreme musculoskeletal pain that it may produce, is a vector borne viral disease. There are four serotypes of virus (DENV 1, 2, 3, 4), transferred by *Aedes Aegypti*.¹⁹ All four serotypes are ubiquitous among Bangladeshis but up until 2025, DENV 3 was the prime type which re-emerged as the prevailing threat again on 2018.^{20,21} Amongst this period DENV 2 and 3 were major circulating type producing outbreaks.²² This infective disease has been the matter of concern worldwide for many years now because of its huge topographical spreading and the public health catastrophe annually. According to World health organization (WHO), maximum dengue case encumbrance is affecting the Western Pacific and Southern Asia.²³ Clinical presentation of dengue differs broadly from asymptomatic infection while others may have flu-like symptoms. Those who have fever suggestive of dengue may have associated headache, retro-orbital pain, backache and many other systemic features like vomiting, diarrhea, organ involvement etc. Patients having features of plasma leakage are supposed to have DHF that may or may not be associated with shock. If sign symptoms of shock are present the ailment is then called dengue shock syndrome.²⁴

This observational study shows a mean age of 26 and 27 years in CDF and DHF groups respectively. Rahman et al show a clear age range (18-33 years) was most affected in their study like ours.⁸ Several previous studies revealed their tints in the 20-40 age group.^{25,26} The number of male patients (69) was higher in two groups than female (44). Some previous studies also observed the male predominance.^{25,27} The duration of hospital stay was 6 to 7 days in both groups. In this study, we show high-risk comorbid conditions like DM (7.9%, 8.1%) and HTN (21.1%, 13.5%). In the recently advanced national guideline, patients with two or more, 'warning signs' got precedence in hospital admission. A higher percentage of 'warning signs' present in the DHF group.

Both of the groups were treated according to symptomatically and supportively. 10 patients did not get any intravenous infusion but rest of all got i/v infusion of about 1000 ml/day. Precautions were taken to avoid fluid overload.²⁸⁻³⁰ Fresh frozen plasma was also given with great care by only 28 patients for the same reason. An RCT shows the effects of fresh frozen plasma on platelet counts in dengue.³¹

Several antibiotics were prescribed according to symptoms. In both groups, cephalosporins were the mostly

prescribed ones (31.6%, 35.1%). Similar findings were shown in several studies.^{28,32,33} This study showed that 51 patients got corticosteroid as shown in a study done by Zhang et al where it was given initially at the treatment to halt DSS.¹² Tranexamic acid was administered in 25 cases in the present study though it is used to control menstrual bleeding as well as GIT bleeding; there is no controlled study on dengue.³⁴ Hematological changes were observed on admission, at 24 hours, 48 hours and 72 hours. Only Thrombocytopenia was statistically significant among all the hematological parameters, similar as previous studies.^{8,25,26,28} This study also focuses on some other lab Investigations especially radiological and ultrasonographical findings. Plural effusion (17.1%), ascites (10.8%), and thick gall bladder wall (2.7%), which were in higher percentage in the DHF group. Ahmed et al, show 17.55% pleural effusion, 16.25% ascites, 16.25% thickened gall bladder wall, and less percentage of organomegaly in their study, which were close to our result.²⁶ But Manam et al found 65.08% thickened gall bladder wall and 49.21% pleural effusion in patients.³⁵

CONCLUSION

Now-a-days dengue has become an alarming viral illness causing sufferings and ailments in lots of people in our country. Classical dengue is more common than hemorrhagic dengue. Thrombocytopenia was evident (significant) in hemorrhagic dengue. Further studies are needed to further evaluation.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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