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Original Article

Pre-Hospital Care and Referral Pattern among Admitted Patients with Dengue Fever in Dhaka Medical College Hospital

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Abstract:

Introduction: *Dengue has become a pressing public health concern for Bangladesh, with a significant rise in the death toll in recent years. Dhaka Medical College Hospital, the largest referral hospital, treats a large number of patients with dengue fever. This study aims to observe prehospital treatment and referral patterns among patients admitted to the hospital with dengue fever.*

Methods: *This observational, cross-sectional study was conducted at Dhaka Medical College Hospital from September 2023 to November 2023, involving patients admitted with dengue infection. All consecutive patients with laboratory-confirmed dengue admitted to one unit (Medicine unit: 3) of the Department of Medicine were included. The data were analyzed using SPSS 25 software.*

Results: *Among the 488 patients, 273 (55.9%) were male. Most patients range in the age group 26-44 (39.5%). The Mean age of patients was 34.16±16.06. The majority, 160 (32.8%) and 123 (25.2%) were homemakers and students, respectively. Most patients (50%, n=244) were diagnosed with Dengue with warning signs (Category B). The mean hospital stay duration was 5.05±2.018 days, and the majority, 438 (89.8%), stayed in the hospital for ≤7 days. The mean ± SD of illness duration was 5.58 ±2.32 days. About 125 (25.6%) patients had co-morbid diseases, and hypertension was the most frequent comorbid condition. The majority of patients, 436 (89.3%) had no co-infections. Eighty-one (16.6%) and 79 (16.2%) patients were treated with antibiotics and papaya leaf extract juice or capsule before hospital admission, respectively, and a few patients used Eltrombopag (2.9%) as well. Among 488 patients, 201 (41.2%) patients were admitted by themselves. Approximately 479 (98.2%) patients survived and were discharged, and five patients died, all of them admitted to the hospital with severe dengue (Category C).*

Conclusion: *A significant portion of patients had practices using medication like antibiotics, steroids, papaya leaf extract juice and eltrombopag, etc., without indication of use. Self-hospitalisation without using a referral system was the most common form of hospitalization among patients with dengue fever.*

Key word: *Dengue Fever, Pre-hospital care, Pre-hospital treatment, Referral pattern, Dhaka, Bangladesh.*

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Introduction

Dengue has recently been assumed to be a public health threat in Southeast Asia, including Bangladesh. It is a vector-born infectious disease of humans caused by dengue virus (DENV), which belongs to the *Flaviviridae* family having four serotypes (DENV serotypes 1–4).[1] Viral transmission occurs between humans by female mosquito species, *Aedes aegypti* and *Aedes albopictus.* Half of the world's population is at risk of dengue infection, with an estimated annual infection of 100 to 400 million, mainly occurring in urban and semi-urban areas of the tropics and subtropics.[2] From 2000 to 2019, the world witnessed a staggering ten-fold increase in reported dengue cases, from 500000 to 5.2 million. 2019 alone saw the highest number of cases reported across 129 countries, indicating a rapid and alarming surge in dengue infections.[3] From 2020 to 2022, reporting of dengue cases declined due to COVID-19, with a rapid resurge over 2022 to 2023.

Although there were sporadic dengue case reports in Bangladesh, accurate transmission and prevalence were not known, and dengue became a disease of public health significance in 2000, with 5,521 officially reported cases and hospital admissions having 93 fatalities.[4,5,6] More than ninety percent of dengue cases were reported in urban areas, and Dhaka was the primary hotspot.[7] Incidence and distribution of dengue correlate with rainfall, and according to data from 2000 to 2017, 49.73% and 49.22% of dengue cases occurred during monsoon and post-monsoon, respectively.[8,9] Heavy rainfall, humidity, rapid unplanned urbanization, and poor waste management have been strong predictors of ecological change, leading to a rapid increase of Aedes mosquitoes, with a massive outbreak of Chikungunya in 2017 and an unprecedented dengue outbreak in 2018 in Dhaka.[9] Round the year transmission and cases of Dengue have increased with increasing reporting of cases in a peri-urban and non-urban area. Cases have increased in peri-urban and nonurban regions.[10]

In Bangladesh, a five-fold increase in reported cases was observed in 2023 compared to 2022.[10] The country has noticed all the serotypes, with DEN2 and DEN3 predominance observed in 2022 and 2023, respectively.[11,12] Secondary infection with a new serotype is associated with severe dengue, which could be an essential factor for the worst-ever death toll. Development of dengue shock syndrome, expanded dengue syndrome, and nonadherence to national guidelines are important factors that were responsible for a high number of deaths.[13] Nonadherence to the national guidelines during hospital management is considered a significant predictor of mortality, and practices of patients with dengue before hospitalization are also crucial.[14] Scientifically sound preventive practices and guideline-recommended practices following the development of dengue fever are significantly lacking.[15] This study aims to observe the practices of patients and practices associated with managing patients with dengue fever before hospitalization.

Methods:

Study Design and Setting

This cross-sectional study was conducted at the Department of Medicine of Dhaka Medical College Hospital. It was conducted from August to November 2023, the peak season for dengue, and targeted all adult admitted dengue cases.

Study Population

This study included all patients aged 13 years and above with laboratory-confirmed dengue infection. Patients were recruited by purposive sampling technique among the admitted cases in a specific unit among the 12 units of the Department of Medicine, Dhaka Medical College Hospital. Informed consent was required from participants, or, in the case of minors and younger (aged under 18), consent was obtained from their legal guardians. Patients or guardians who refused to provide consent were excluded.

Laboratory-confirmed dengue cases were defined as the presence of acute febrile illness in patients along with a combination of two or more of the following symptoms: headache, retro-orbital or ocular pain, myalgia, arthralgia, rash, a positive tourniquet test (defined as the presence of >20 petechiae per 1 inch2), or leukopenia (defined as a white blood cell count of 5,000 cells/mm3), coupled with a positive result for NS1 antigen or dengue-specific IgM and IgG serology. Patients were categorized according to national guidelines into Category-A, Category-B and Category-C.(16)

Category-A dengue cases were defined as dengue cases without any warning signs, comorbidity, or evidence of shock syndrome.

Category-B dengue cases were patients with dengue and warning signs or comorbid conditions requiring hospitalization. Warning signs included abdominal pain or tenderness, persistent vomiting (vomiting with signs of dehydration); clinical fluid accumulation; bleeding from mucosal areas including the nose, gums, gastrointestinal tract, or vagina; lethargy; restlessness; liver enlargement of more than 2 cm; and increased hematocrit (>20%) concurrent with a rapid decrease in platelet count (<100,000 platelets/mL). Severe dengue was defined as having (i) severe plasma leakage, defined as plasma leakage with shock or respiratory distress (respiratory rate 24 breaths/minute with oxygen saturation,95% in room air and/or requiring oxygen therapy);

(ii) severe clinical bleeding, defined as spontaneous bleeding from mucosal areas that necessitated a blood transfusion; or (iii) severe organ involvement, defined as AST >1,000 IU/L and/or ALT >1,000 IU/L, serum creatinine levels two times or more above baseline, myocarditis, and/or encephalitis.

Category C dengue includes cases with severe plasma leakage leading to shock and intense bleeding, requiring urgent medical intervention.

Data Collection

All the physicians of the respected unit of the Medicine Department were adequately trained for data collection. Data were collected using a structured questionnaire administered during face-to-face interviews with patients or their guardians. The questionnaire included socio-demographic characteristics, clinical history, and details about pre-hospital treatment. Additional clinical data about in-hospital treatment and outcomes were obtained from patient management files and laboratory reports. The questionnaire was translated into the local language and back-translated to ensure accuracy. A pilot test was carried out to assess the reliability and clarity of the questionnaire.

Ethical Statement: Before commencing the study, formal ethical approval was obtained from the Institutional Review Board (IRB) of Dhaka Medical College Hospital.

Results:

A total of 488 patients were included in the study, among those admitted to a single Medicine Unit during the study period. About 56% of patients were male, and the mean age (±SD) of patients was 34.16 (±16.06). Among the different occupations, the majority, 160 (32.8%) and 123 (25.2%), were homemakers and students, respectively. Among 488 patients, the highest age range was 26-44 years old (39.5%) (Table 1).

Table 1. Socio-demographic characteristics of Dengue patients (n=488) and their clinical presentation during admission

Attributes	Frequency (n)	Percentage (%)
Gender		
Female	215	44.1
Male	273	55.9
Age group (in years)		
13-17=Late Adolescents	62	12.7
18-25 =Young Adult	111	22.7
26-44=Adult	193	39.5
45-59=Middle Age	69	14.1
60 -85=Old age	53	10.9
Mean ± SD= 34.16±16.06 (min-max=13-85)		
Occupation		
Business	45	9.2
Daily wager, Farmer, Fisherman, Garment worker	52	10.7
Homemaker	160	32.8
Private job	87	17.8
Student	123	25.2
Unemployed	21	4.3
Religion		
Islam	467	95.7
Hinduism	21	4.3
Diagnosis		
Dengue fever (DF)-Uncomplicated (Cat A)	35	7.2
Dengue with warning sign-Cat B	244	50.0
DF with significant hemorrhage	16	3.3
DHF III & IV	2	0.4
DHF with significant hemorrhage	22	4.5
Expanded Dengue Syndrome	21	4.3
Expanded Dengue Syndrome, Metabolic and electrolyte abnormalities	2	0.4
Severe Dengue -Cat C	146	29.9
Presence of any co-morbidity	125	25.6

[DHF III & IV - Dengue hemorrhagic fever grade III and IV]

Half of the patients (n=244) were admitted with dengue with warning signs (Category B), and a significant number of patients (30%, n= 146) were admitted with severe dengue (Category C). Other presentations included DHF with significant hemorrhage (4.5%n=22), Expanded Dengue Syndrome (4.3%, n=21), DF with significant hemorrhage (3.3%=16), and DHF III & IV (n=2). Dengue Syndrome with Metabolic and electrolyte abnormalities (n=2) (Table 1).

After hospitalization, the Mean (± SD) duration of hospital stay was 5.05 (±2.018) days, and the majority, 438 (89.8%), were admitted ≤7 days in the hospital. The mean (± SD) duration of illness was 5.58 ±2.32 days, and about 125 (25.6%) patients had co-morbid diseases or conditions. Among the co-morbid diseases, Hypertension (7.2%, n=35), Diabetes (5.3%, n=26), combined Hypertension, and Diabetes (6.1%, n=30) were common, and 10 (2%) patients were admitted with pregnancy (Table 2). About ten percent of patients had co-infection, and enteric fever was the most common (2.9%, n=14). (Table 3)

Table 2. Distribution of co-morbid diseases among dengue patients (n=125)

Co-morbidity	frequency (n)	percentage (%)
Chronic liver disease (CLD)	2	0.4
Diabetes	26	5.3
Hemoglobinopathies and Thalassemia	4	0.8
Hypertension	35	7.2
Hypertension, Diabetes	30	6.1
Acute Cholecystitis	2	0.4
Bronchial Asthma	2	0.4
Hypertension, Diabetes, Chronic kidney disease (CKD)	4	0.8
Hypertension, Diabetes, Ischemic Heart Disease (IHD)	3	0.6
Hypertension, Heart Failure	2	0.4
Hypertension, Ischaemic Stroke	1	0.2
Hypertension, Ischemic Heart Disease (IHD)	4	0.8
Pregnancy	10	2.0

Table 3: Co-infection among Dengue patients (n=400)

Co-infection	Frequency (n)	Percentage (%)
Acute Cholecystitis	2	0.4
Enteric fever	14	2.9
Gluteal Abscess	2	0.4
No coinfection	436	89.3
Pancreatitis	2	0.4
Peuperal Sepsis	1	0.2
Pneumonia/ ARI	14	2.9
Pneumonia/ ARI, Sepsis	2	0.4
Puerperal sepsis	1	0.2
UTI	14	2.9

Self-admitted patients were most common among all admitted cases (41.2%, n=201). Upazila Health Complex, District Hospital, and private hospital referrals were about 25.4%, 13.9%, and 16.2%, respectively (Table 4).

Table 4. Distribution of referral places of patients (n=488)

Referral Places	Frequency (n)	Percentage (%)
District Hospital	68	13.9
Medical College	10	2.0
Private Hospital	79	16.2
Self	201	41.2
Self, UHC, Private Hospital	2	0.4
Specialized Institute	4	0.8
UHC	124	25.4

A substantial number of patients received both unnecessary and inappropriate pre-hospital treatment. Antibiotics were used by 16.6% (n=81) of patients, papaya leaf extracts by 16.2% (n=79), and steroids by 4.7% (n=23). Eltrombopag, an expensive and unendorsed therapy, was utilised by 2.9% (n=14) of patients (Table 5)

Table 5: Pre-hospital treatments of Dengue patients (n=400)

Pre-Hospital Treatments	Frequency (n)	Percentage (%))
Steroid		
Yes	23	4.7
No	465	95.3
NSAID		
No	488	100.0
Antibiotics		
Yes	81	16.6
No	407	83.4
Eltrombopag		
Yes	14	2.9
No	474	97.1
Papaya Leaf extract juice or capsule		
Yes	79	16.2
No	409	83.8

Among the 488 patients, 98.2% (n=479) survived and were discharged, while 1% (n=5) died. Patients diagnosed with severe dengue (Category C) account for all fatalities. There was a statistically significant correlation between age and outcome ($p < 0.01$), with the highest fatality rate (7.5%, n=4) among elderly patients aged 60–85 years. No deaths were observed in Category A or Category B patients (Table 6,7).

Table 6. Outcome of admitted Dengue patients (n=400)

Outcome of Patients	Frequency (n)	Percentage (%)
Patient died	5	1.0
Patient survived and discharged	479	98.2
Referred to other hospital	4	0.8
Patient died	5	1.0

No significant association was found between duration of hospital stay and the outcome of patients ($p>0.01$) The association between the severity of the disease (as classified by warning signs) and patient outcomes was found to be statistically significant ($p<0.01$). Patients in Group C (severe dengue) had the highest mortality and referral rates, while those in Group B had the most favourable outcomes, with no recorded deaths or referrals. This indicates that the severity of dengue, based on the presence of warning signs, plays a critical role in determining patient outcomes, with more severe cases leading to higher mortality rates and hospital referrals (Table 7).

Table 7. Association between risk factors with patients' outcome (n=400)

Attribute	Patients' Outcome			
	Patient died	Patient survived and discharged	Referred to other hospital	Significance
Age & sex				
13-17	0 (0)	62 (100)	0 (0)	<0.01
18-25	0 (0)	109 (98.2)	2 (1.8)	
26-44	1(0.5)	190 (98.4)	2 (1)	
45-59	0 (0)	69 (100)	0 (0)	
>60-85	4 (7.5)	49 (92.5)	0 (0)	
Duration of Hospital stay				
≤7 days	3 (0.7)	431 (98.4)	4 (0.9)	0.071
>7 days	2 (4)	48 (96)	0 (0)	
Category of patients based on warning signs				
Group A (mild; dengue without warning sign)	0 (0)	35 (94.6)	2 (5.4)	<0.01
Group B (dengue with warning signs or comorbidity or coinfection)	0 (0)	265 (100)	0 (0)	
Group C (severe dengue)	5 (2.7)	179 (96.2)	2 (1.1)	

Discussion:

Of the 488 patients, the majority were male (55.9%), and the mean age was about 34 years. Half of the patients were admitted with dengue with warning signs (Category-B), and one-third were admitted with severe dengue (Category-C). The mean duration of illness before hospitalization was 5 days, and about 90% of patients were discharged before 7 days of hospitalization. One-quarter of patients were admitted with co-morbid disease or condition, and hypertension and diabetes were highest among them. A high proportion of patients (41.2%) bypassed any referral system. A significant portion, 16.6% and 16.2% of patients had been treated with antibiotics and papaya leaf extract (juice or capsules), respectively, before hospital admission. Five patients (1%) died, all from severe dengue (Category C). Mortality was higher among older patients (ages 60-85), with a significant association between patient age, severity of dengue, and outcome.

During the 2023 dengue outbreak, the highest frequency of cases was found among the 19 – 29 age group, and male-female ratio was 3:2.[17] Male patients were higher in this study, and as adult patients were admitted to the Department of Medicine, the mean age was higher, similar to a study from a nearby tertiary hospital in Dhaka.[18] Patients with uncomplicated dengue (Category-A) are treated at home with antipyretic and supportive care and are advised to come to the hospital if any warning signs develop. According to national guideline patients with Category B and Category C dengue are hospitalized; most were in these two categories. The mean duration before hospitalization is about five days, indicating that the patient may present with a critical phase or stage of plasma leakage, which develops mainly during the stage of defervescence.[19]

As the largest tertiary hospital in the country, patients with dengue fever from various parts of Bangladesh and different co-morbid conditions or diseases are admitted to Dhaka Medical College Hospital. Notably, the use of a referral system is poor, a characteristic of the country's healthcare practice.[19] In addition to co-morbid disease, in patients with pregnancy, co-infection was also present. The incidence of co-infection with dengue among hospitalized patients during the endemic period in Bangladesh is unknown. In this study, enteric co-infection is about 10% and enteric co-infection is 2.9% and co-infection of enteric and dengue in hospitalized patients is as high as 7.8% in the surrounding country.[20] The use of antibiotics is higher than that of proven infections, as self-medication with antibiotics is high in the country.[21] Though there is no well-designed controlled clinical trial of the efficacy and safety of papaya leaf extract in dengue, many patients got papaya leaf extract or capsule as pre-hospital medication, and few of the patients got eltrombopag which is costly and not also recommended for dengue management.

Five patients (1%) died among the patients, all of whom suffered from severe dengue. Mortality was higher among older patients (ages 60-85), with a significant association between patient age, severity of dengue, and outcome. Secondary infection is an independent risk factor for severe dengue, and older age increases the cumulative risk of secondary infection.[22] In the 2023 dengue outbreak, those over 30 comprised less than 40% of total dengue patients, but 64% of mortality occurred in this group.[23] Disease severity significantly influenced patient outcomes, particularly in those categorized with severe dengue (Category C), who showed the highest mortality and referral rates. Duration of hospital stay showed no significant correlation with mortality.

Conclusion

This study highlights the widespread use of papaya leaf extract or capsule, antibiotics, steroids, etc., as prehospital medication, which is not recommended by national guideline. Self-hospitalization was common mode of hospitalization, which indicates a poor referral system. Health education to increase public awareness regarding guideline-recommended pre-hospital practice, training of healthcare associates to stratify patients based on clinical risk, timely referral of patients, and strengthening of the referral system are essentials to improve the clinical outcome of dengue patients.

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