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Evaluation of Death from Dengue Syndrome - Study of 60 Cases in a Tertiary Hospital of Bangladesh

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Abstract

Background: Dengue fever presents a significant public health challenge in tropical regions, including Bangladesh. This study aims to evaluate the clinical characteristics and outcomes of severe dengue syndrome cases leading to mortality in a tertiary hospital setting. The aim of the study was also to identify the factors related to mortality in Dengue Syndrome. **Material & Methods:** This retrospective study involved 60 dengue patients who expired during treatment at Bangabandhu Sheikh Mujib Medical College Hospital, Faridpur, Bangladesh, from June 2023 to December 2023. Patient demographics, clinical presentations, treatment initiation time, fluid management, and time from treatment to death were analyzed. **Results:** Dengue Shock Syndrome was the most common subtype (46.67%). The study population had a broad age distribution and a higher prevalence of females (60%). Most patients sought medical attention after 3-7 days of fever. Blood pressure variations at admission included hypotension and non-recordable readings, common in severe dengue. Vomiting and shortness of breath were prevalent worsening symptoms. Treatment initiation was often delayed, with 43.33% experiencing a 16-30-minute delay post-admission. Thrombocytopenia was notable, especially in severe dengue cases. Fluid management was generally inadequate, particularly in the critical initial hours of treatment. Mortality occurred rapidly post-treatment initiation, with 50% dying one day after treatment began. **Conclusions:** The study highlights the need for early recognition and prompt management of dengue fever, especially in severe cases. Inadequate fluid management was a significant concern, emphasizing the need for adherence to established guidelines. These findings provide crucial insights into dengue management in Bangladesh, underlining the necessity of improving and following clinical protocols to enhance patient outcomes.

Keywords:- Dengue fever, Dengue Shock Syndrome, Fluid management, Mortality.

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INTRODUCTION

Dengue fever represents a major global health challenge, with an estimated 100 million cases and 500,000 cases of its severe form, dengue hemorrhagic fever (DHF), occurring annually worldwide, leading to approximately 25,000 deaths.[1] This viral disease, caused by the dengue virus, a member of the Flaviviridae family, is primarily transmitted by Aedes aegypti mosquitoes and is prevalent in over 100 endemic countries, putting almost half of the world's population at risk.[2] The clinical manifestation of dengue ranges from a mild, nonspecific febrile illness to severe and fatal hemorrhagic disease. The severity of dengue fever and its progression to more dangerous forms like DHF and dengue shock syndrome (DSS) depend on several factors, including viral serotype and strain, the individual's age, immune status, and genetic predisposition.[1] Typical symptoms of dengue include fever, headache, myalgia, arthralgia, and skin rashes, with severe forms characterized by increased vascular permeability, hemorrhage, and shock. Secondary infections with different dengue virus serotypes are considered major risk factors for developing severe dengue disease, a hypothesis supported by the model of immunopathogenesis, which suggests a significant role played by the cascade of cytokines.[2,3] In the context of Bangladesh, the history of dengue reflects a pattern of increasing prevalence and severity. The country has witnessed large epidemics, the largest of which occurred in 2019, suggesting an urgent need for a deeper understanding of dengue's dynamics within this specific context.[4,5] A significant characteristic of dengue in Bangladesh is its broad demographic impact, affecting various age groups, with both children and adults experiencing severe forms such as DHF/DSS.[5,6] Environmental factors, notably seasonal climatic changes, significantly influence the transmission dynamics of dengue in Bangladesh.[7,8] Mortality rates from dengue fever show variability across different geographic regions, with countries like Bangladesh experiencing a higher burden.[9] DHF and DSS, the severe manifestations of dengue, are major contributors to this mortality, often resulting in plasma leakage, organ failure, and sometimes death.[10,11] Several studies have identified risk factors for severe dengue, highlighting demographics (age, gender, ethnicity), pre-existing health conditions (diabetes, hypertension), and certain immunological responses.[3,12] Moreover, the role of cytokines, such as macrophage migration inhibitory factor (MIF) and interleukin-10 (IL-10), has been emphasized, with their elevated serum levels being associated with severe disease outcomes.[13,14] Despite these developments, there remains a notable gap in the literature, particularly in understanding the specific patterns, demographic details, and clinical outcomes of dengue-related deaths in Bangladesh. This lack of detailed, localized data is a significant impediment to the formulation of effective public health strategies and clinical management protocols tailored to the unique epidemiological and clinical characteristics of dengue fever in the Bangladesh context.[15,16] Addressing this gap is crucial for enhancing our understanding of the disease and improving the prevention, diagnosis, and treatment of dengue. In response to this need, our study aims to closely

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examine and evaluate the characteristics and outcomes of dengue syndrome cases leading to mortality in a tertiary hospital setting in Bangladesh. By focusing on this specific aspect of the disease, we hope to provide valuable insights into the clinical patterns of dengue fever, the risk factors associated with its severe forms, and the key demographic and clinical indicators that can predict the likelihood of mortality in dengue patients. This approach is particularly relevant given the complex interplay of demographic, environmental, and viral factors that contribute to the severity and outcomes of dengue fever.[17,18] Understanding these elements is not only critical for addressing the current challenges posed by dengue fever in Bangladesh but also for contributing to the global body of knowledge on this increasingly prevalent disease.

MATERIAL AND METHODS

This retrospective study was conducted at the Department of medicine, Bangabandhu Sheikh Mujib Medical College Hospital, Faridpur, Bangladesh. The study duration was from June 2023 to December 2023. It involved a sample size of 60 dengue patients who unfortunately expired during their treatment at the hospital. Data of the samples collected from treatment sheets of succumbed dengue patients, stored in record keeper. All participants included in this study were confirmed cases of dengue, indicated by a positive Dengue NS1 antigen test, and had been admitted to the hospital for dengue management. Patients in the study were categorized into two groups based on their clinical condition at the time of admission. Category 1 (Cat-1) included patients who presented with non-palpable pulse and non-recordable blood pressure. According to the National guideline for the management of dengue fever, these patients required aggressive fluid management, necessitating at least 1-2 liter of fluid within the first hour. The recommended types of fluids for Cat-1 patients included colloids like Dextran 40, Plasmasol, Plasma, Human albumin, Hemaceel, Blood, or Blood components. Over a 24-hour period, the fluid requirement was a minimum of 1 liter per hour until the patient's condition improved. Category 2 (Cat-2) patients were identified by a palpable pulse and recordable blood pressure. The initial treatment for these patients should involve administering at least 500 ml-1 liter of fluid in the first hour, with the preferred fluids being Normal Saline (NS) or 5% Dextrose in Normal Saline (DNS). For the following 24 hours, the guideline recommended a continuous fluid administration rate of at least 500 ml per hour, with Dextran 40 or Plasmasol in worsening cases. An important aspect of the study was to evaluate the adherence to these national guidelines in fluid administration. Patients who did not receive the recommended amount of fluid as per the guidelines were categorized under "Inadequate". All collected data of the participants were organized in to a structured database and were analyzed using SPSS V.25.

RESULTS

The age of participants was broadly spread across different decades of life. Specifically, individuals aged 21-30, 31-40, and 41-50 each constituted 18.33% of the sample, making these age groups the most represented. Those aged 51-60 and 61-70 each made up 11.67%, while the least represented age groups were 71-80 years and those over 80, each accounting for

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5% and 8.33%, respectively. The youngest age group (≤20 years) also made up 8.33% of the sample. The Mean±SD age of the participants was calculated to be 47.23±21.1 years. Regarding gender distribution, the study had a higher representation of females, accounting for 60% of the participants, compared to males, who made up 40% of the sample.

Most participants experienced fever for 3-4 days and 5-7 days before admission, accounting for 46.67% and 43.33% of the cases, respectively. A smaller proportion, 6.67%, had a fever lasting 1-2 days, while only 3.33% experienced fever for more than 7 days. The Mean±SD duration of fever before hospital admission was 4.50±1.77 days.

Blood pressures were classified according to American college of Cardiology. For systolic blood pressure, hypotension and non-recordable measurements were the most common, each occurring in 28.33% of the participants. Normal systolic blood pressure was observed in 23.33% of the cases. Elevated systolic blood pressure and Hypertension Stage 1 were noted in 10% and 6.67% of the participants, respectively, while Hypertension Stage 2 was present in 3.33% of the cases. In terms of diastolic blood pressure, the highest percentage (33.33%) of participants had normal readings. Both hypotension and non-recordable diastolic blood pressure were observed in a significant portion of the participants, accounting for 18.33% and 28.33%, respectively. Hypertension Stage 1 diastolic blood pressure was present in 8.33% of the participants, while Hypertension Stage 2 was noted in 6.67%. Elevated diastolic blood pressure was the least common, found in only 5% of the cases. [Table 2]

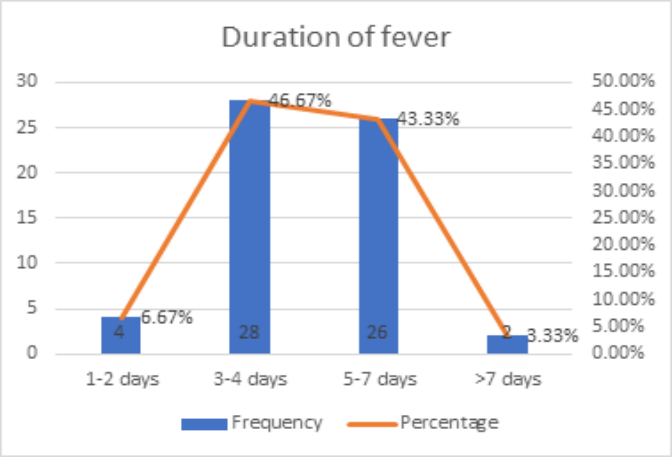

Figure 1: Distribution of fever duration before admission among the participants (N=60)

The distribution of worsening symptoms alongside fever in the 60 participants showed a range of additional clinical features. Vomiting was the most commonly reported symptom, experienced by 36.67% of the participants. Shortness of breath was also relatively common, reported by 16.67% of the cases. Other symptoms included abdominal pain (8.33%), diarrhea (10.00%), and less frequently, bloody vomit (3.33%), restlessness (3.33%), and jaundice (1.67%). A notable portion of the participants, 13.33%, experienced symptoms that were categorized as 'others,' indicating a diversity of clinical presentations not captured by the more common categories. Interestingly, a small percentage (6.67%) of the participants did not report any worsening symptoms alongside fever. [Table 3]

The distribution of the delay between admission and the start of treatment among the 60 participants varied, with most patients experiencing a delay of 16-30 minutes,

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accounting for 43.33% of cases. A significant number of participants, 28.33%, had a delay of 31-45 minutes. Delays of ≤15 minutes and 46-60 minutes were each observed in 10.00% of the participants. Longer delays in treatment initiation, ranging from 1-2 hours, were less common, noted in 5.00% of the cases. Very few participants experienced delays of 2-3 hours and over 3 hours, each category accounting for 1.67% of the participants. The mean ±SD delay time in starting treatment after admission was calculated to be 45.42±93.12 minutes. [Table 4]

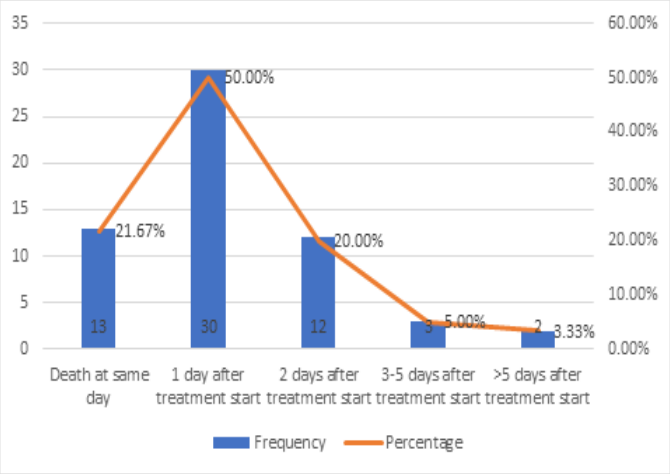

Figure 2: Distribution of participants by gap between treatment start and death (N=60)

Half of the participants (50%) succumbed to the illness one day after the start of treatment, indicating a rapid progression of the disease post-treatment. A significant number of participants, 21.67%, died on the same day they received treatment, underscoring the severity of their condition upon admission. An additional 20% of the participants passed away two days after treatment began. A smaller percentage, 5%, died between 3 to 5 days after treatment initiation, while only 3.33% of the participants lived for more than 5 days after starting treatment. The Mean±SD duration from the start of treatment to death was 1.35±1.58 days.

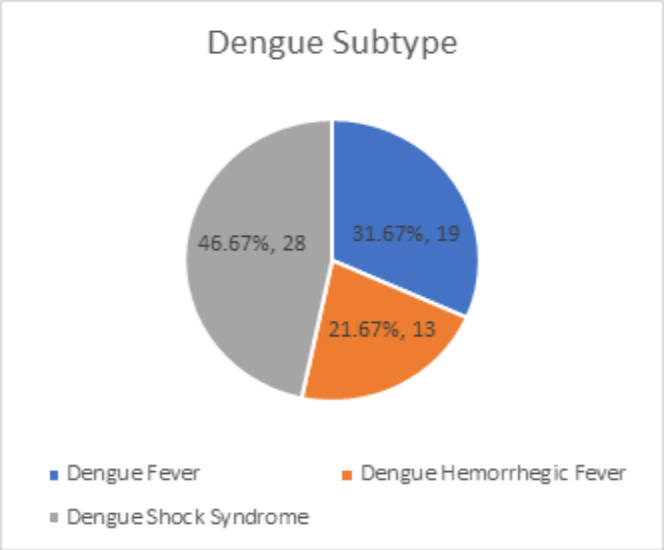

Figure 3: Distribution of participants by dengue subtypes (N=60)

In this study of 60 dengue patients, the distribution of dengue subtypes revealed that the majority, 46.67%, were diagnosed with Dengue Shock Syndrome (DSS). Dengue Fever (DF), the less severe form, was present in 31.67% of the cases, while Dengue Hemorrhagic Fever (DHF) was observed in 21.67% of the participants.

In the comparison of mean platelet counts among different dengue subtypes in the study, notable differences were observed. Patients with Dengue Fever (DF) had a higher mean platelet count of 72,868.42, with a standard deviation of 29,089.824. In contrast, those with Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) had significantly lower mean platelet counts, 43,615.38 (SD: 19,024.276) and 44,785.71 (SD:

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17,157.996), respectively. The statistical analysis showed a p-value of 0.004, indicating a significant difference in platelet counts between these dengue subtypes. [Table 5]

The distribution of fluid administration among the 60 dengue patients revealed that a significant majority received inadequate fluid in the first hour of treatment, accounting for 80%. Only 20% of the participants received an adequate amount of fluid initially. The most commonly administered fluid in the first hour was Normal Saline, used in 73.33% of cases, followed by 5% Dextrose in Normal Saline and Plasmasol, each given to 10% of patients. Lesser-used fluids included Citrated Saline and Hypertonic Saline, each administered to 3.33% of the participants. The pattern of inadequate fluid administration continued over the first 24 hours, with 88.33% of patients not receiving the adequate amount. Only 11.67% received an adequate fluid amount during this period. Normal Saline remained the most frequently used fluid, administered to 75% of the patients, followed by Plasmasol at 13.33%. Other fluids like Citrated Saline, 5% Dextrose in Normal Saline, Hypertonic Saline, and Manisol were used less frequently. [Table 6]

Table 1: Distribution of participants by baseline characteristics (N=60)

Variables	**Frequency**	**Percentage**
Age		
<=20	5	8.33%
21-30	11	18.33%
31-40	11	18.33%
41-50	11	18.33%
51-60	7	11.67%
61-70	7	11.67%
71-80	3	5.00%
>80	5	8.33%
Mean±SD	47.23±21.1	
Sex		
Male	24	40.00%
Female	36	60.00%

Table 2: Distribution of blood pressure among participants at admission (N=60)

Blood pressure	**Frequency**	**Percentage**
Systolic		
Hypotension	17	28.33%
Normal	14	23.33%
Elevated	6	10.00%
Hypertension Stage 1	4	6.67%
Hypertension Stage 2	2	3.33%
Non-recordable	17	28.33%

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Diastolic		
Hypotension	11	18.33%
Normal	20	33.33%
Elevated	3	5.00%
Hypertension Stage 1	5	8.33%
Hypertension Stage 2	4	6.67%
Non-recordable	17	28.33%

Table 3: Distribution of worsening symptom among the participants (N=60)

Worsening Symptoms	**Frequency**	**Percentage**
Vomiting	22	36.67%
Shortness of Breath	10	16.67%
Abdominal Pain	5	8.33%
Bloody Vomit	2	3.33%
Diarrhea	6	10.00%
Jaundice	1	1.67%
Restlessness	2	3.33%
Others	8	13.33%
No	4	6.67%

Table 4: Distribution of participants by gap between admission and treatment start (N=60)

Treatment delay	**Frequency**	**Percentage**
≤15 minutes	6	10.00%
16-30 minutes	26	43.33%
31-45 minutes	17	28.33%
46-60 minutes	6	10.00%
1-2 hour	3	5.00%
2-3 hour	1	1.67%
>3 hours	1	1.67%
Mean±SD	45.42±93.12 minutes	

Table 5: Comparison of Mean±SD platelet among different dengue subtypes (N=60)

Dengue Subtypes	**Mean**	**SD**	**p-value**
Dengue Fever	72868.42	29089.824	0.004
Dengue Hemorrhagic Fever	43615.38	19024.276	
Dengue Shock Syndrome	44785.71	17157.996	

Table 6: Distribution of participants by fluid given (N=60)

Fluid Given (amount and type)	**Frequency**	**Percentage**
Fluid at 1st hour		
Adequate	12	20.00%

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Inadequate	48	80.00%
Type of Fluid given at 1st hour		
5% Dextrose in Normal Saline	6	10.00%
Citrated Saline	2	3.33%
Hypertonic Saline	2	3.33%
Normal Saline	44	73.33%
Plasmasol	6	10.00%
Fluid at 24 hour		
Adequate	7	11.67%
Inadequate	53	88.33%
Type of Fluid given at 24 hour		
Citrated Saline	3	5.00%
5% Dextrose in Normal Saline	2	3.33%
Hypertonic Saline	1	1.67%
Normal Saline	45	75.00%
Plasmasol	8	13.33%
Manisol	1	1.67%

DISCUSSION

In this retrospective study focusing on dengue patients in Bangladesh, the analysis of patient demographics, clinical presentations, and management strategies yields significant insights, especially when juxtaposed with global research findings. The age and sex distribution in our cohort, with a broad age range and a higher female prevalence, mirrors global trends in dengue, reflecting the widespread impact of the disease across demographics. This aligns with the findings of Zahoor et al. (2019), which suggest dengue's indiscriminate effect on all age groups and genders.[19]

The duration of fever prior to hospital admission in our study, predominantly ranging from 3 to 7 days, corresponds with the typical clinical progression of dengue fever where the fever phase lasts approximately this duration. Phakhounthong et al. (2018) emphasized the importance of prompt medical attention within this period, which is crucial for managing severe dengue complications effectively.[20] Variations in blood pressure at admission, particularly instances of hypotension and non-recordable measurements, signify the hemodynamic alterations common in dengue, primarily in its severe forms. The presence of worsening symptoms like vomiting and shortness of breath alongside fever in our study aligns with the established warning signs for severe dengue, necessitating careful monitoring and timely intervention. Heilman et al. (2014) discussed the significance of these symptoms as indicators of the progression towards severe dengue, highlighting the need for vigilant clinical monitoring in such cases.[21] Concerning the treatment delay observed in our study, the significant gap between hospital admission and the start of treatment raises concerns, especially given the rapid progression of dengue in severe cases. This

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echoes the findings of Wongchidwan et al. (2018), who emphasized the detrimental impact of treatment delays in exacerbating the severity of dengue, underlining the critical need for prompt and effective management in such cases.[22] The interval from the initiation of treatment to death in our patients, particularly the high incidence of mortality within a day of treatment onset, indicates the aggressive nature of the disease. This rapid disease progression post-treatment initiation is in line with findings from Abello et al. (2016), who observed similar rapid progression in severe dengue cases, stressing the necessity of timely intervention.[23] The study's findings on varying platelet counts across different dengue subtypes, with lower counts observed in more severe forms like Dengue Hemorrhagic Fever and Dengue Shock Syndrome, reflect the hematological impacts of the dengue virus. Costa et al. (2015) similarly noted a correlation between thrombocytopenia and disease severity in their study, highlighting this as a common feature in dengue infections.[24] However, perhaps the most crucial aspect of our study is fluid management in severe dengue cases. Our findings indicated a significant prevalence of inadequate fluid administration, particularly in the first 24 hours of hospital admission. Proper fluid management is critical in severe dengue, as it directly impacts the patient's hemodynamic stability and is essential in countering the effects of plasma leakage. In severe cases, this can progress to shock and multiple organ failure if not managed appropriately. Hung (2012) highlighted the use of isotonic crystalloid solutions, and in more severe cases, colloids for their osmotic effect. However, they also carry a risk of adverse events such as fluid overload and respiratory distress, which must be carefully balanced.[25] Wongsa (2015) underscored that in hemodynamically unstable patients, crystalloids should be the initial choice of fluid, with a switch to colloids if necessary, underscoring the need for careful fluid therapy.[26]

In conclusion, our study's insights into the clinical characteristics and management of dengue, particularly in severe cases, align with global research findings. They underscore the complexities of managing this disease, highlighting the critical need for early intervention, appropriate fluid management, and close monitoring of clinical signs to improve patient outcomes in severe dengue infections.

Limitations of the Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSIONS

The current study provides valuable insights into the clinical presentation and management of dengue fever in a tertiary care setting in Bangladesh. Our findings underline the broad age and gender distribution of dengue, indicating its widespread impact across various demographics. The observed delay in seeking medical attention, with most patients presenting several days after the onset of fever, emphasizes the need for public awareness about the importance of early healthcare engagement. Blood pressure variations and the presence of worsening symptoms, such as vomiting and shortness of breath, were noted as crucial indicators of disease progression,

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necessitating vigilant monitoring and timely medical intervention. One of the most significant findings of this study is the inadequate fluid management during the critical initial hours of treatment, highlighting a gap in adherence to dengue management protocols. This aspect is particularly concerning given the pivotal role of fluid therapy in the prognosis of severe dengue cases. Our study stresses the necessity of judicious and appropriate fluid management, aligned with current guidelines, to mitigate the risk of complications such as shock and organ failure.

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