

Prognostic Insights: Mortality Prediction in Dengue Patients at a Tertiary Care Center

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Abstract

Introduction: Dengue fever, a globally pervasive mosquito-borne viral infection, poses a significant health threat, particularly in tropical regions. While often presenting as a self-limiting febrile illness, a subset of patients can progress to severe forms, necessitating a deeper understanding of mortality predictors. This study explores critical factors such as severe plasma leakage, thrombocytopenia, age, and comorbidities that influence mortality in dengue patients. Recognizing these predictors is vital for early intervention, significantly impacting patient outcomes.

Materials and Methods: In this study at NAMO Medical Education and Research Institute, Silvassa, we explored mortality predictors in dengue patients from January 1 to December 30, 2022. Our inclusive approach covered all ages and genders. Ethically approved, the study involved a meticulous review of medical records, assessing demographics, clinical data, and comorbidities. Patient evaluations included history, physical exams, and lab tests. Descriptive statistics and various tests identified mortality predictors. This comprehensive methodology unveils the intricate dynamics of mortality prediction in dengue patients.

Results: In our study of 100 subjects, we observed a mean age of 40.2 ± 15.2 years, with 59% males and 41% females. The mean hospital stay was 5.5 ± 3.2 days, and complications were reported in 39%, with an overall mortality rate of 11%. Comparing 11 non-survivors to 89 survivors, non-survivors were older (49.2 ± 18.5 years vs. 37.4 ± 15.3 years, $P = 0.01$) and exhibited higher rates of leukocytosis, elevated CRP, and acute kidney injury. Our univariate and multivariate analyses identified age, leukocytosis, and acute kidney injury as potential predictors of mortality, emphasizing their significance in determining outcomes in dengue patients.

Conclusion: our study identifies advanced age, leukocytosis, elevated CRP, and acute kidney injury as significant predictors of mortality in dengue fever patients. These findings underscore the complexity of dengue prognosis and emphasize the importance of a multifaceted approach in clinical assessments.

Key words: Dengue Mortality, Predictive Factors, Age and Dengue

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Introduction

Dengue fever, a mosquito-borne viral infection caused by the dengue virus, poses a significant global health threat, particularly in tropical and subtropical regions. [1] While the majority of dengue cases manifest as a self-limiting febrile illness, a subset of patients can progress to severe forms of the disease, leading to increased morbidity and mortality. [2] Understanding the predictors of mortality in patients with dengue fever is crucial for early identification and intervention, ultimately improving patient outcomes. [3]

Several factors have been identified as key predictors of mortality in individuals with severe dengue. One of the primary indicators is the presence of severe plasma leakage, leading to a condition known as dengue shock syndrome (DSS). [4,5] This occurs when the vascular permeability increases, resulting in fluid extravasation from blood vessels and subsequent hypovolemic shock. [6] Monitoring hematocrit levels and assessing for signs of plasma leakage are essential in identifying patients at risk for DSS.⁵ Additionally, thrombocytopenia, characterized by a low platelet

count, is a common feature in severe dengue and serves as another predictor of adverse outcomes.⁷ Platelet dysfunction and coagulopathy contribute to complications such as bleeding, which can be life-threatening. [3,7]

Furthermore, the age of the patient has been recognized as a significant factor influencing mortality in dengue fever. [8] Children and the elderly are particularly vulnerable, with studies indicating that extreme age groups may experience more severe manifestations of the disease. [9] The immune response to dengue virus infection may vary with age, affecting the clinical course and outcome. [10] Comorbidities such as diabetes, cardiovascular disease, and immunosuppressive conditions have also been associated with an increased risk of mortality in dengue patients. [11] These underlying health conditions can exacerbate the severity of the disease and hinder the body's ability to mount an effective immune response. [11]

Unraveling the predictors of mortality in patients with dengue fever is pivotal for identifying high-risk individuals and implementing timely interventions. Clinicians and healthcare providers must remain vigilant for signs of severe dengue, including plasma leakage, thrombocytopenia, and the influence of age and comorbidities on disease severity. Early recognition and appropriate management of these factors can significantly impact patient outcomes and reduce the global burden of severe dengue-related mortality. [12]

Material and Methods

The study employed an analytical, cross-sectional study design to investigate the predictors of mortality in patients admitted for the management of dengue fever at the Department of Internal Medicine, NAMO Medical Education and Research Institute, Silvassa. The study covered the period from January 1, 2022, to December 30, 2022, capturing a one-year timeframe to provide a comprehensive overview of patient cases during this period.

The study included all patients admitted to the Department of Internal Medicine with a confirmed diagnosis of dengue fever during the specified time frame. Inclusion criteria comprised patients of all ages and both genders, ensuring a broad representation of the population seeking medical care for dengue fever. Exclusion criteria were limited to cases where complete medical records were unavailable or when patients had a coexisting condition that could significantly impact the outcomes. The study protocol was submitted to and approved by the institutional ethics committee of NAMO Medical Education and Research Institute.

Data were collected through a thorough review of medical records, including demographic

information, clinical presentations, laboratory results, comorbidities, and outcomes. The severity of dengue was assessed based on the World Health Organization (WHO) criteria, distinguishing between dengue fever and severe dengue. [13] Specific attention was given to identifying predictors of mortality, including but not limited to age, presence of plasma leakage, thrombocytopenia, and underlying comorbidities.

Upon admission, a comprehensive assessment of each patient included a thorough examination of their medical history and a physical examination. Additionally, basic laboratory investigations were conducted for all patients, with requests sent to the hospital laboratory. At the initial evaluation, key parameters such as age, gender, white blood cell count (WBC), platelet count, serum C-reactive protein (CRP) level, serum alanine aminotransferase (ALT) level, and serum creatinine were systematically recorded. In the context of this study, thrombocytopenia was characterized by a platelet count falling below 30,000/mcL, while leukocytosis was defined as a WBC exceeding 11,000/mcL. Elevated CRP levels were identified when the concentration surpassed 5 mg/dL, acute liver injury was determined by ALT levels exceeding 200 IU/L, and acute kidney injury was established when serum creatinine levels rose above 1.5 mg/dL.

The patient's hospital stay duration and any complications arising from dengue fever were meticulously documented throughout the course of their care. Each patient's outcome was classified into two categories: survivors, denoting those who successfully recovered and were discharged from the hospital, and non-survivors, encompassing individuals who unfortunately succumbed to the illness during their hospitalization.

Descriptive statistics were employed to summarize demographic characteristics and clinical features of the study population. Continuous variables were presented as means with standard deviations or as medians with interquartile ranges, depending on the distribution. Categorical variables were expressed as frequencies and percentages. To identify predictors of mortality, appropriate statistical tests such as chi-square tests, t-tests, or logistic regression analysis were performed based on the nature of the variables.

Results

In a study involving 100 subjects, the mean age was 40.2 ± 15.2 years, with 59% male and 41% female participants. The mean duration of hospital stay was 5.5 ± 3.2 days. Majority of the patients were from lower socio-economical class (79%) belongs to the rural areas (82%). Complications, as detailed in Figure 1, were reported in 39% of the patients with overall mortality rate of 11% among 100 study subjects.

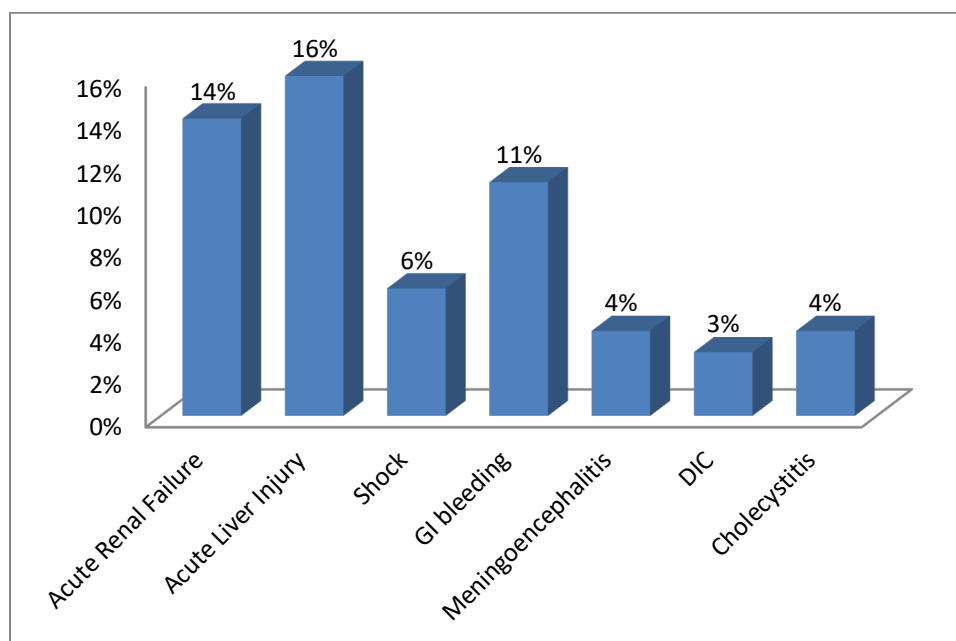


Figure 1: Complications among subjects (n=100)

In our study, we compared 11 non-survivors to 89 survivors. Non-survivors had a significantly higher mean age (49.2 ± 18.5 years) than survivors (37.4 ± 15.3 years), with a P value of 0.01. Those above 40 years constituted a higher percentage among non-survivors (72.73%) compared to survivors (68.54%, $P = 0.002$). Non-survivors showed a higher prevalence of leukocytosis ($> 11,000/\text{mcL}$) at 63.64%, contrasting with 42.70% among survivors

($P = 0.0013$). All non-survivors had elevated CRP ($> 5 \text{ mg/dL}$), significantly different from 66.29% in survivors ($P = 0.012$). Non-survivors also exhibited a higher incidence of acute kidney injury (creatinine $> 1.5 \text{ mg/dL}$) at 45.45%, compared to 10.11% in survivors, with a P value of 0.01. Other parameters did not differ significantly between non-survivors and survivors.

Table 1: Clinical and Laboratory Parameters among survivors and non-survivors

Variables	Non- Survivors (n=11)	Survivors (n=89)	P value
Mean age Mean \pm SD (years)	49.2 ± 18.5	37.4 ± 15.3	0.01
Age more than 40 years (%)	8 (72.73%)	61 (68.54%)	0.002
Age up to 40 years (%)	3 (27.27%)	28 (31.46%)	
Male gender (%)	6 (54.55%)	53 (59.55%)	0.412
Female gender (%)	5 (45.45%)	36 (40.45%)	
Duration of hospital stay, Mean \pm SD (days)	6.5 ± 10.3 days	5.1 ± 4.1 days	0.532
Thrombocytopenia ($< 30,000/\text{mcL}$)	5 (45.45%)	36 (40.45%)	0.342
No Thrombocytopenia	6 (54.55%)	53 (59.55%)	
Leukocytosis ($> 11,000/\text{mcL}$)	7 (63.64%)	38 (42.70%)	0.0013
No Leukocytosis	4 (36.36%)	61 (67.42%)	
Elevated CRP ($> 5 \text{ mg/dL}$)	11 (100%)	59 (66.29%)	0.012
No CRP elevation	0	30 (33.71%)	
ALT $> 200 \text{ U/L}$	3 (27.27%)	13 (14.61%)	0.721
No Acute Liver Injury	8 (72.73%)	76 (85.39%)	
S. creatinine $> 1.5 \text{ mg/dl}$	5 (45.45%)	9 (10.11%)	0.01
No Acute Kidney Injury	6 (54.55%)	80 (89.89%)	

In Table 2, our study explored predictors for survival through univariate and multivariate analyses. The analysis revealed that individuals aged > 40 years had significantly lower odds of survival, indicating age as a potential factor influencing outcomes (OR: 0.150, 95% CI: 0.030 – 0.600, $P = 0.01$). However, in the multivariate analysis, while the trend

persisted, the association was not statistically significant (OR: 0.305, 95% CI: 0.060 – 1.525, $P = 0.232$). Leukocytosis, when present, was associated with reduced odds of survival in both univariate (OR: 0.200, 95% CI: 0.060 – 0.800, $P = 0.02$) and multivariate analyses (OR: 0.220, 95% CI: 0.040 – 1.100, $P = 0.031$), suggesting its potential role as a

predictor for poorer outcomes. Additionally, the presence of acute kidney injury significantly lowered the odds of survival in both univariate (OR: 0.120, 95% CI: 0.030 – 0.500, P = 0.001) and

multivariate analyses (OR: 0.145, 95% CI: 0.025 – 0.830, P = 0.01), highlighting its importance as a critical factor associated with decreased survival rates in our study population.

Table 2: Predictors of survival

Variables		Univariate analysis		Multivariate analysis	
		OR (95% CI)	P values	OR (95% CI)	P value
Age group	<40 years				
	≥40 years	0.150 (0.030 – 0.600)	0.01	0.305 (0.060 - 1.525)	0.232
Leukocytosis	Present	0.200 (0.060 – 0.800)	0.02	0.220 (0.040 – 1.100)	0.031
	Absent				
Acute Kidney Injury	Present	0.120 (0.030 – 0.500)	0.001	0.145 (0.025 – 0.830)	0.01
	Absent				

Discussion

The majority of cases of dengue present as a self-limiting febrile illness, a subset of patients may progress to severe forms, leading to heightened morbidity and mortality. Predicting mortality in dengue patients is crucial for early intervention and improved outcomes. Factors such as severe plasma leakage, thrombocytopenia, age, and comorbidities have been identified as key predictors, underscoring the importance of unraveling these dynamics for effective clinical management and public health strategies.

Our study involved 100 subjects with a mean age of 40.2 ± 15.2 years, comprising 59% males and 41% females. A study by Mahmood et al. [14], who studied 115 patients, our age distribution aligns with the majority being up to 45 years old, similar to their population (71.3%, mean age 38.40 ± 18.1 years). However, our study reported a slightly longer mean duration of hospital stay (5.5 ± 3.2 days) compared to Mahmood et al. [14] (4.6 ± 3.4 days). Our study focused on a younger population with a mean age of 40.2 years, whereas recent study by Lee et al. [15] observed deceased patients with a median age of 73.9 years.

Our study revealed a notable association between advanced age and increased mortality, supported by Mahmood et al.'s [14] findings where survivors were significantly younger than non-survivors. However, contrasting results from Bhaskar et al. [16] and Khalil et al. [17] suggested that age might not universally serve as a predictor of mortality in dengue. In our study, the odds of survival were significantly lower for individuals aged >40 years, a trend consistent with Malhi et al.'s [18] observations, emphasizing the risk associated with ages above 50 years. Similarly, Macias et al. [19] underscored that older patients face a higher risk of death from dengue, and the impact of comorbidities further complicates the scenario.

The heightened vulnerability of elderly individuals to infection-related mortality and morbidity is well-established due to age-related functional decline in

immunity and physiological changes affecting organ systems. [20] This vulnerability is exacerbated by the presence of comorbidities, which can worsen the course of dengue virus infection. [21] The consistency in findings across studies [22,23], despite variations in demographics and methodologies, reinforces the notion that age is a critical determinant of mortality in dengue. Advanced age, often accompanied by a decline in physiological functions and the presence of comorbidities, appears to create a scenario where the body's ability to combat the virus is compromised, leading to increased mortality. [24,25]

In our study, a thorough examination of patients with dengue fever revealed distinctive patterns between non-survivors and survivors. Notably, non-survivors exhibited a considerably higher prevalence of leukocytosis ($> 11,000/\text{mcL}$) at 63.64%, in stark contrast to the 42.70% observed among survivors (P = 0.0013). The statistical significance of this difference was further underscored by the univariate (OR: 0.200, P = 0.02) and multivariate analyses (OR: 0.220, P = 0.031), emphasizing the potential role of leukocytosis as a robust predictor for adverse outcomes.

Additionally, the presence of acute kidney injury emerged as another critical factor associated with decreased odds of survival. Both univariate (OR: 0.120, P = 0.001) and multivariate analyses (OR: 0.145, P = 0.01) consistently demonstrated the significance of acute kidney injury in predicting mortality among our study population. The stark contrast in outcomes between non-survivors and survivors underscores the importance of monitoring and addressing kidney function in dengue cases.

Elevated C-reactive protein (CRP) levels (> 5 mg/dL) were universally present in all non-survivors, a notable departure from the 66.29% prevalence observed among survivors (P = 0.012). This finding aligns with the growing recognition of CRP as a potential biomarker for predicting severe disease and poor outcomes in dengue fever, as

supported by similar observations in literature. [26,27]

Comparing our results with Lee et al.'s [15] study on chronic kidney disease (CKD) patients infected with dengue, we find a parallel emphasis on the prognostic significance of leukocytosis. Their multivariate analysis highlighted leukocytosis as independently correlated to in-hospital mortality, reinforcing our observation of leukocytosis as a critical predictor. [14]

The convergence of our findings with Mahmood et al.'s [14] study further bolsters the evidence for the predictive value of leukocytosis, elevated CRP, and acute kidney injury. Their significant observations in these areas at the time of admission align with our results, creating a consistent narrative across studies. [28–30]

While previous studies, such as Karunakaran et al. [31] and Ho TS et al. [32], have highlighted the association of leukopenia with dengue severity, our study and others, including Thein et al. [33] and Almas et al. [34], emphasize the distinctiveness of leukocytosis in predicting mortality. This disparity underscores the need for a nuanced understanding of different hematological parameters in the context of dengue outcomes. Medagama et al.'s [35] findings on the predictive value of elevated CRP in predicting severe outcomes in dengue fever echo our study's results, reinforcing the potential utility of CRP as a valuable clinical marker.

While our study did not explicitly delve into thrombocytosis, it is essential to consider its counterpart, thrombocytopenia, as a common feature in dengue fever. [36] Thrombocytopenia has been widely recognized as a hallmark of severe dengue cases, emphasizing the importance of platelet count monitoring. [37,38] Thein et al.'s [33] observations and Almas et al.' [34] s study align with this, emphasizing that non-survivors had a significantly lower platelet count at the time of presentation. The interplay between thrombocytopenia and thrombocytosis warrants further investigation, especially in understanding their dynamic roles in predicting outcomes.

Our study did not explicitly explore liver involvement; however, liver dysfunction is a recognized aspect of severe dengue. Mahmood et al.'s [14] study highlighted a significantly higher prevalence of acute liver injury among non-survivors. It is crucial to interpret our findings in tandem with this observation, recognizing the interconnectedness of liver function with other factors in influencing the overall prognosis in dengue fever.

In interpreting our findings, the multifaceted nature of dengue fever becomes evident. Leukocytosis, acute kidney injury, and elevated CRP consistently

emerged as predictors of adverse outcomes, aligning with the observations of various studies. [23,27,31] Thrombocytopenia, frequently reported in severe cases, and acute liver injury further contribute to the complexity of the disease.³⁶

Our data, while not explicitly addressing thrombocytosis or liver involvement, underscores the importance of a holistic approach in understanding the intricate dynamics of dengue fever. The interconnected nature of these clinical parameters emphasizes the need for a comprehensive assessment in clinical practice, moving beyond isolated markers to grasp the nuanced progression of the disease.

Despite contributing valuable insights into predictors of mortality in dengue patients, our study has certain limitations. The single-center design may limit the generalizability of findings, and variations in patient demographics or healthcare practices could affect results. Additionally, the retrospective nature of the study relies on available medical records, possibly leading to incomplete data or underreporting of certain variables. The study's timeframe may not capture potential evolving trends, and the absence of a control group limits the ability to establish causal relationships.

Conclusion

In conclusion, our study's integration with the broader literature on dengue fever provides a nuanced understanding of the prognostic indicators, emphasizing the need for a multifactorial approach in predicting outcomes. Leukocytosis, acute kidney injury, elevated CRP, thrombocytopenia, and liver involvement collectively contribute to the intricate landscape of dengue fever, urging clinicians to consider the synergistic impact of these factors in guiding patient management and interventions.

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