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PREDICTORS OF HOSPITAL STAY AND PROGNOSTIC FACTORS FOR DENGUE INFECTION IN HOLY FAMILY HOSPITAL, RAWALPINDI

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ABSTRACT

Background: The spread of dengue virus infection (DVI) is due to the increase in trade and tourism, which has inadvertently spread the virus from endemic regions to other parts of the world. Recent epidemics in Pakistan have shown that the virus can cause significant health problems but there is a scarcity of data on the factors associated with increased hospital stay and mortality in DVI.

Objective: To identify and develop predictive models for the length of hospital stay and the risk of complications in patients with dengue infection.

Methods: The Department of Infectious Diseases, Holy Family Hospital, Rawalpindi, Pakistan, conducted this retrospective cohort study. The study spanned three months, and it comprised a sample size of 122 patients. Inclusion criteria involved patients admitted to the hospital with diagnoses of dengue infection, dengue hemorrhagic fever, or dengue shock syndrome, with their diagnoses confirmed through serology. Patients below 12 years of age and those with incomplete demographic information were excluded from the study.The association between outcomes, such as length of hospital stay (LOS), and other variables, was examined using chi-squared tests for categorical variables and Student's t-test for continuous variables. Binary logistic regression was employed to estimate odds ratios and their corresponding 95% confidence intervals concerning hospital stay duration (≤3 days versus >3 days).

Results: The study included 122 DVI patients, with a mean age of 42.06 years. The most common age group affected was 50-65 years old. Twenty-four patients had diabetes and 15 had hypertension. Eighty-six patients had DF, 28 had DHF, and 8 had DSS. Eleven patients developed respiratory failure and 18 had acute renal injury. The mortality rate was 4.1%. The mean LOS was 4.65 days. The study found that older age, co-morbid conditions, severity of infection, and end organ injury were all predictors for longer length of stay (LOS) in patients with DVI. Patients with DSS had the longest LOS, followed by patients with DHF and then patients with DF. Patients with higher levels of ALT or lower levels of platelets were also more likely to have a longer LOS. End organ injury, such as acute kidney injury, central nervous system injury, or respiratory injury, also significantly affected LOS.

Conclusion: The predictors of hospital stay and prognostic factors for dengue infection are a complex and evolving field of research. However, some of the most important factors that have been identified include age, severity of infection, co-morbid conditions and derangement in laboratory parameters.

Keywords: dengue virus infection, length of stay, dengue hemorrhagic fever, dengue shock syndrome

INTRODUCTION

Dengue virus infection is a mosquito-borne viral infection, prevalent in tropical and subtropical regions globally.[1] The dengue virus exists in four serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), and infection with one serotype does not provide lifelong immunity to the others.[2] Following a mosquito bite, symptoms of dengue typically emerge within 3-14 days.[3] Common manifestations include high fever, headache, muscle and joint pain, nausea, vomiting, and a rash. In certain instances, the disease can progress to a more severe form known as dengue hemorrhagic fever (DHF), characterized by low blood pressure, bleeding, and organ failure. DHF can be fatal, especially among children.[3]

For many years, Pakistan has faced the challenge of dengue virus infection as a significant public health issue. The initial confirmed outbreak of dengue fever in the country dates back to 1994, followed by a sudden surge in cases and an annual epidemic trend, starting in Karachi in November 2005.[4] Subsequently, Pakistan has experienced multiple substantial dengue outbreaks, notably in 2011, 2013, 2016, and 2019.[5,6] Among these, the 2019 outbreak stands as the most extensive in the country's history, accounting for over 100,000 cases and resulting in 100 fatalities.

Pakistan's health system lacks sufficient preparedness to manage extensive dengue outbreaks. Understanding the factors linked to extended hospital stays and mortality in patients with DVI is crucial for enhancing patient care. Currently, there is a dearth of literature addressing this issue. As a response to this gap, this study was formulated to explore and pinpoint potential factors that could influence the duration of hospitalization and mortality rates among patients with DVI.

MATERIALS & METHODS

This retrospective study was conducted at department of medicine in Holy Family Hospital in Rawalpindi, Pakistan. Th eligibility criteria for included patients comprised of following; admitted with a diagnosis of DVI, DF, DHF, DSS with confirmation of diagnosis through serology testing. Patients under the age of 12 and those with incomplete demographic details were excluded. Furthermore, if any patients had serology negative for DVI or was found to have concomitant typhoid fever or malarial infection, he was also excluded from study.

A profroma was designed which collected data on demographic details of patients, their co-morbids, findings from laboratory results, length of hospital stay, documentation about severity of infection and any end organ injury or mortality. As previously many researchers have have reported that patients of DVI have a median hospital stay of 3-4 days, hence, patients in our study were divided into either LOS<3 days or $\geq$ 3days.[4]These two groups were compared to identify variables that might predict an increased LOS.

The dengue virus infection was classified into dengue fever , dengue hemorrhagic fever and dengue shock syndrome by employing the WHO classification of 1997.[7] Hospital stay was defined as more than one day of bed occupancy in the hospital. Mortality was defined as death within 14 days of admission. Dengue virus infection was defined as the presence of the virus confirmed by serology. Dengue hemorrhagic fever was defined as fever, hemorrhagic manifestations, and thrombocytopenia along with evidence of plasma leakage. Acute kidney injury was defined according to the AKI network classification.[8]

After obtaining ethical approval from the hospital ethical review committee, data collection commenced. Baseline values and demographic data were summarized using descriptive statistics. Mean and standard deviation were used for quantitative data, while frequencies with percentages were applied for qualitative data. The association between outcomes, such as length of hospital stay (LOS), and other variables, was examined using chi-squared tests for categorical variables and Student's t-test for continuous variables. Binary logistic regression was employed to estimate odds ratios and their corresponding 95% confidence intervals concerning hospital stay duration (≤3 days versus >3 days). Variables that demonstrated an impact in predicting hospital stays lasting over 3 days in the univariate analysis were incorporated in the formulation of the multivariable models. All p-values were derived from two-sided tests, and a significance level of less than 0.05 was set. The analyses were conducted using SPSS (Statistical Package for the Social Sciences) version 23.

RESULTS

The study included 122 DVI patients who fulfilled inclusion criteria. Among these cases, 79 (64.8%) were males, while 43 (35.2%) were females with mean age of the patients being 42.06±15.92 years. When data was stratified acceding to age groups, it was found that mostly affected age group was between 50-65 years of age comprising 29.5% of all subjects. This was followed by 35-50 and 18-35 years age group comprising 27.9% and 27.0% of patients. No significant gender based predominance was found in any specific age group (p=0321).

When patients were assessed about posible risk factors 24(19.7%) had diabetes and 15(12.3%) had hypertension. Regarding distribution of dengue fever it was found that 86 (70.5%) had DF, 28 (23.0%) had DHF, and 8 (6.6%) had DSS. 11 patients (9%) develop respiaratory failure. Most commonly observed drawback was acute renal injury occuring in 18(14.75%) patients. Mortality rate was observed to be 4.1% with 5 patients loosing their life in the mostly having associated risk factors of advancing age and comorbididtis like hypertension and diabetese. Patients included in our study had mean ALT levels of 179.24± 21.54. The platelet counts in our data ranged from aminimum value of 29,000 to a maximum of 180,000, with a mean of coount of platelets being 94,646 and a standard deviation of 43,609.

Mean length of stay in our study was 4.65±2.54 days with minimum being 1 day and maximum limit of 12 days. When data was grouped according length of stay, we found that 35.2% of the pateints had less than 3 days, 27.0% had stay between 3 to 5 days, 18.9% had length of stay between 5-7 days and 18.9% had more than 7 days o stay.

Table 1 shows the results of a study that investigated the predictors for length of stay (LOS) in patients with dengue virus infection (DVI). The table shows the LOS for patients with DVI who were <3 days and >3 days, as well as the P value for each variable. Patients who were >65 years old were more likely to have a longer LOS than patients who were <35 years old (p value of 0.034). The participants with co-morbid conditions like Diabetes Mellitus and hypertension (were more likely to have a longer LOS than patients without these ailments(p=0.031).Length of stay increased with severity of infection as patients with DSS were more likely to have a longer LOS than patients with dengue fever or DHF (p-value=0.021). Furthermore, during workup if patients had higher levels of ALT or lower levels of platelets, they were more likely to have a longer LOS (p= 0.043). End organ injury also significantly affected LOS as patients with acute kidney injury, central nervous system injury, or respiratory injury were more likely to have a longer LOS.

Table 1: Predictors for length of stay in DVI

Variable	Length of stay		P value
	<3 days	>3 days	
Age			
● Mean Age	31.67±8.54	54.21±6.32	
● 12-18 years	7(16.27%)	3(3.79%)	0.034
● 18-35	23(53.48%)	10(12.65%)	
● 35-50	5(11.62%)	29(36.7%)	
● 50-65	5(11.62%)	31(39.24%)	
● >65	3(6.97%)	6(7.59%)	
Gender			
● Male	30(69.76%)	49(62.02%)	0.891
● Female	13(30.23%)	30(37.98%)	
Comordbidty			
● DM	3(13.04%)	20(86.94%)	0.031
● HTN	2(13.33%)	13(86.66%)	
DVI Type			
● DF	41(93.35%)	45(56.96%)	
● DHF	2(4.65%)	26(32.91%)	0.021
● DSS	0	8(10.12%)	
Laboratory Values			
ALT			
● ALT <45	23(53.48%)	3(3.79%)	
● ALT 45-100	18(41.86%)	30(37.97%)	0.043
● ALT 100-200	2(4.65%)	12(15.18%)	
● ALT 200-500	0	25(31.64%)	
● ALT>500	0	9(11.39%)	
Platelets			
● Platelets= <50,000	1(2.32%)	16(20.25%)	
● Platelets= 50,000-100,000	9(20.93%)	45(56.96%)	0.037
● Platelets=100,000-150,000	14(32.55%)	13(16.45%)	
● Platelets= >150,000	19(44.18%)	5(6.32%)	
End Organ Injury			
● AKI	2(11.11%)	16(88.89%)	
● CNS	1(9.09%)	10(90.91%)	0.001
● Respiartory	0	11(100%)	

DISCUSSION

Dengue virus infection (DVI) is a mosquito-borne illness that is endemic in tropical and subtropical regions around the world. The virus is spread through the bite of an infected *Aedes aegypti*mosquito.[9] DVI can range in severity from a mild, flu-like illness to a life-threatening condition. In recent years, there has been an increase in the number of DVI cases reported worldwide. This is due in part to the increased movement of people and goods between countries, which has facilitated the spread of the virus.[10] In Pakistan, there have been several large-scale DVI epidemics in recent years.[5,6] These epidemics have highlighted the need for better understanding of the factors that contribute to increased hospital stay and mortality in patients with DVI. The objective of this study was to identify and develop predictive models for the LOS and the risk of complications in patients with dengue infection. The study was conducted at the Department of Infectious Diseases, Holy Family Hospital, Rawalpindi, Pakistan.

This retrospective cohort study was conducted over a period of three months. The study population included all patients who were admitted to the hospital with a diagnosis of dengue infection, dengue hemorrhagic fever (DHF), or dengue shock syndrome (DSS) during the study period. A total of 122

patients were included in the study. The mean age of the patients was 42.06 years. The most common age group affected was 50-65 years old. Twenty-four patients had diabetes and 15 had hypertension. Eighty-six patients had DF, 28 had DHF, and 8 had DSS. Eleven patients developed respiratory failure and 18 had acute renal injury. The mortality rate was 4.1%.

Older age, co-morbid conditions, severity of infection, and end organ injury were all predictors for longer LOS. Patients with DSS had the longest LOS, followed by patients with DHF and then patients with DF. Patients with higher levels of ALT or lower levels of platelets were also more likely to have a longer LOS. End organ injury, such as acute kidney injury, central nervous system injury, or respiratory injury, also significantly affected LOS. In other words, patients who were older, had co-morbid conditions, had a more severe infection, or had end organ injury were more likely to have a longer LOS. Additionally, patients with higher levels of ALT or lower levels of platelets were also more likely to have a longer LOS. This finding is consistent with past studies that have shown that older patients tend to have more severe forms of dengue and may require extended hospital care.[11-16] Co-morbid conditions can also complicate the management of dengue and increase the overall LOS. Patients with more severe infections require more intensive care and treatment, which can prolong the hospital stay. End organ injury can also be serious and can require prolonged treatment, which can also lead to a longer LOS.

Several studies have shed light on the clinical factors and manifestations associated with dengue virus infection. Limkittikul et al. (2016) discovered that patients with advanced age (above 65 years), elevated white blood cell count (greater than 10,000/μL), low platelet count (less than 50,000/μL), and those experiencing Dengue Hemorrhagic Fever or Shock tended to have longer hospital stays.[11] In a study by Kumar et al. (2015), common clinical manifestations observed in dengue patients admitted to a tertiary care hospital in India included fever, headache, myalgia, arthralgia, and rash.[12] Halstead (2007) provided an extensive overview of dengue, stating that the infection's severity ranges from mild febrile illness to life-threatening Dengue Hemorrhagic Fever.[13] Lee et al. (2018) highlighted that elderly patients with dengue hemorrhagic fever were at higher risk of fatality if they exhibited characteristics such as age above 75 years, comorbid conditions, low platelet count, and high hematocrit.[14] Oliveira et al. (2017) found that dengue hemorrhagic fever in Brazil was associated with features like age below 15 years, male sex, history of previous dengue infection, and urban area of residence.[15] Additionally, Huy et al. (2019) conducted a meta-analysis and identified factors linked to dengue shock syndrome, including age below 15 years, male sex, history of previous dengue infection, and severe dengue.[16]

It can be concluded from findings of our study that the combination of advancing age, co-morbid conditions, derangement in laboratory parameters and severity of infection at presentation along end organ injury could be associated with a longer LOS. These patients were more likely to require advanced therapies, such as renal replacement therapy or ventilator support, which delayed their discharge from the hospital.

We recognize numerous limitations in our study. The data collection process was retrospective, potentially introducing bias towards patients with more severe conditions, as they were more likely to be captured and recorded in the system. Ideally, we would have preferred to prospectively grade dengue hemorrhagic fever, enabling early detection of undetected cases, but this was not possible with our current coders. Furthermore, variations in admission and discharge criteria among different clinicians caring for these patients could have influenced our findings. To comprehensively assess factors associated with mortality, a larger patient cohort would be necessary. Additionally, our study focused on adult patients, limiting its generalizability to pediatric populations. It's essential to recognize that this study was conducted at a single center, and its results may not be representative of the entire population

CONCLUSIONS

The study found that the most common risk factors for longer length of stay in patients with dengue virus infection were advanced age, co-morbid conditions, severity of infection, and end organ injury. Patients who were >65 years old, had diabetes Mellitus or hypertension, had DSS, had higher levels of

ALT or lower levels of platelets, or had acute kidney injury, central nervous system injury, or respiratory injury were more likely to have a longer LOS. The findings of this study can be used to help clinicians identify patients who are at risk for longer LOS and to develop strategies to reduce LOS in patients with DVI.

DISCLOSURE

The study was conducted in accordance with the Declaration of Helsinki. All participants were informed about the study and their consent was obtained before any data was collected. The data collected was kept confidential and was not shared with any third parties without the participant's consent. The participants were free to withdraw from the study at any time.

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