

DEVELOPMENT OF A PIMS SPECIFIC DENGUE HEPATITIS SEVERITY SCORE: A RETROSPECTIVE CROSS SECTIONAL STUDY OF EMR DATA

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ABSTRACT

Objective: To develop and evaluate a simple PIMS-specific Dengue Hepatitis Severity Score using routinely available clinical variables.

Study design: Retrospective cross-sectional study.

Place and duration of study: Pakistan Institute of Medical Sciences (PIMS), Islamabad, 06 months (June to November 2025).

Methodology: This study was conducted using electronic medical records (EMR) of patients of ≥ 13 years of age, with lab-confirmed dengue infection and hepatic involvement. The patients were categorized into severe and non-severe dengue hepatitis groups. Independent predictors were identified using multivariate logistic regression, and a clinical severity score was developed. Receiver operating characteristic (ROC) curve analysis was used to evaluate diagnostic performance.

Results: Total patients in this study were 97. Bleeding (OR = 11.24), hypotension (OR = 6.99), and hepatomegaly (OR = 5.95) were independent predictors of severe dengue hepatitis ($p < 0.05$). A three-point severity score was constructed (0–3). The score demonstrated good discrimination with an AUC of 0.761 (95% CI: 0.659–0.863). A cut-off ≥ 1 showed sensitivity of 77.1% and specificity of 71.0%.

Conclusion: The PIMS Dengue Hepatitis Severity Score is a simple, bedside tool that effectively identifies patients at risk of severe disease. It can be helpful for early triage and clinical decision-making, although external validation is required before general use.

Key words: Dengue, Hepatitis, Risk Assessment, Severity of Illness Index.

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INTRODUCTION

Dengue fever is among the most significant mosquito-borne viral infections on the planet, the geographical distribution of which is rapidly expanding and the disease burden is growing exponentially in tropical and subtropical areas. According the World Health Organization (WHO), hundreds of millions of

dengue cases are reported every year, and a significant part of these develop into serious disease that needs hospital admission and intensive care^{1,2}. In South Asia, including Pakistan, dengue outbreak is still a significant burden of on the healthcare systems³.

The hepatic involvement is a frequent and clinically relevant symptom of dengue infection. There is a tendency of mild to moderate rise in transaminases. Some patients develop dengue hepatitis, with significant increase of enzymes, hepatomegaly, jaundice, coagulopathy. In rare cases, acute liver failure occurs^{4,5}. Dengue liver injury pathogenesis is multifactorial, comprising the direct viral cytopathic effects, immune-mediated hepatocellular injury, hypoxic injury because of shock, and the systemic inflammatory responses⁶.

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A number of studies have revealed that dengue patients with hepatic dysfunction are at high risk of bleeding, shock, long hospital stay, and death^{7,8}. High Aspartate aminotransferase (AST) levels, hepatomegaly, and clinical instability have been continuously linked to adverse outcomes⁹. Nevertheless, the increasing awareness of dengue hepatitis as a significant complication has not been accompanied by a simple clinical scoring system, one that is widely accepted and solely targeted to predict severe dengue hepatitis based on the use of bedside variables.

Early detection of patients who are at risk of worsening is essential to optimize monitoring intensity, resource allocation, and avoid negative outcomes, especially in resource-constrained environments. The majority of the current dengue severity models use complicated laboratory parameters or imaging results that might not be easily accessible in practice⁵.

In this context, no simple dengue hepatitis-specific bedside scoring system currently exists to predict severe hepatic involvement using routinely available clinical variables, particularly in resource-limited settings like South Asian populations. The present study aimed to develop and evaluate a Pakistan Institute of Medical Sciences (PIMS)-specific Dengue Hepatitis Severity Score using routinely available clinical features in adolescents and adults with dengue-associated hepatic involvement. This study aims to enhance early risk assessment and facilitate prompt clinical decision-making in hospitalised dengue patients by developing a simple, practical bedside tool.

METHODOLOGY

This was a retrospective, cross-sectional study, done at the Department of General Medicine, PIMS, Islamabad, from June 2025 to November 2025. After obtaining institutional ethical approval, electronic medical records (EMR) were reviewed for the purpose of developing and validating a dengue hepatitis severity scoring system. The study included patients aged ≥ 13 years who were diagnosed with lab-confirmed dengue infection; non-structural protein 1 (NS1) antigen and/or dengue antibody (IgM); and hepatic involvement, characterized by high AST or alanine aminotransferase (ALT) levels ≥ 100 U/L. Pregnant patients, patients having pre-existing chronic liver disease, viral hepatitis, concomitant viral infections, taking hepatotoxic drugs, or incomplete EMR were excluded. A consecutive sampling method was used.

The sample size of 96 was calculated with the WHO calculator by keeping the confidence interval of 95%, anticipated prevalence of dengue-associated liver involvement 48%, and absolute precision of 10%¹⁰. A total of 97 eligible patients fulfilling the

CAPSULE SUMMARY

A simple PIMS-specific Dengue Hepatitis Severity Score was developed and evaluated, using routinely the available clinical variables. It effectively identified patients at risk of severe disease, which can be helpful for early triage and clinical decision-making, although external validation is required before general use.

inclusion criteria were included in the final analysis, which met and slightly exceeded the calculated sample size.

Taking into account the study objectives and relevant literature, a structured proforma was designed for data collection retrospectively from the EMR system of the PIMS. It included demographic characteristics, clinical presentation, laboratory findings, and outcome variables. To ensure data quality, all extracted records were reviewed for completeness and consistency. Patients with missing clinical / laboratory information were excluded. Data were entered into a password-protected database. To minimize transcription errors before statistical analysis the data were cross-checked by a second investigator.

The main outcome variable was severe dengue hepatitis, defined as “dengue-associated hepatic involvement (ALT/AST ≥ 100 U/L) accompanied by one or more indicators of severe clinical deterioration during hospitalization, which are admission to a high-dependency or intensive care unit, development of hepatic failure, or in-hospital mortality”. Patients not meeting the above-mentioned criteria were placed in the category of having non-severe dengue hepatitis. Independent variables were demographic profile (age and sex), clinical features on admission (bleeding manifestations, hypotension and hepatomegaly), and laboratory parameters (platelet count, serum albumin, AST, ALT, serum bilirubin). Bleeding manifestations were recorded as the presence of clinically documented mucosal, gastrointestinal, or other hemorrhagic events. Hypotension was defined as systolic blood pressure < 90 mmHg or documentation of hemodynamic instability in the medical record. Hepatomegaly was determined based on the finding of clinical examination documented by the treating physician where the liver edge is palpable > 2 cm below the right costal margin during deep inspiration, or when the total liver span exceeds 12 to 15 cm upon percussion in the midclavicular line. These variables were extracted from EMR and evaluated as potential predictors of severe dengue hepatitis.

Variables demonstrating clinical relevance and statistical significance were entered into the multivariable logistic regression model for development of the Dengue Hepatitis Severity Score. The severity of dengue hepatitis was determined, using the severity of dengue hepatitis recorded during the course of hospitalization. Patients with a severe outcome were identified as those who experienced significant clinical deterioration that necessitated advanced care, whereas those who did not were considered non-severe.

IBM SPSS Statistics version 23 was used to analyze data. Continuous variables were checked in terms of normality and presented in the form of mean \pm standard deviation or median

with interquartile range (IQR), respectively. Frequencies and percentages were used to depict categorical variables. The Mann-Whitney U test (for continuous variables) and the Chi-square test of association (for categorical variables like bleeding, hypotension, hepatomegaly), were applied to make comparisons between severe and non-severe groups. A multivariate binary logistic regression model was used to enter variables of clinical relevance and get the results as odds ratios (ORs) with 95 percent confidence interval (CI). A Dengue Hepatitis Severity Score was constructed based on the key predictors found in multivariate analysis; 1 point each for bleeding, hypotension, and hepatomegaly was assigned in order to facilitate clinical applicability and ease of bedside use. The overall score was between 0 and 3. The analysis performed was a receiver operating characteristic curve (ROC) analysis to evaluate the discriminative ability of the severity score and to determine the optimum cut-off value. Diagnostic performance was determined using sensitivity, specificity, and area under the curve (AUC). A p-value of less than 0.05 was regarded as being statistically significant.

RESULTS

The sample size was 97 patients. The participants had a mean age of 49.19 ±19.10 years, and their ages ranged between 13 and 80 years. The study population was females, comprised of slightly majority (51.5%), and males, 48.5% (Table 1).

Serum bilirubin and liver enzymes were high and were highly suggestive of hepatic involvement. Thrombocytopenia was prevalent. Serum albumin was within normal range. Results of lab tests indicate the presence of significant hepatic dysfunction in the subjects of the study (Table 1).

The platelet counts were found to be lower in the patients with severe dengue hepatitis than in the non-severe group, but this was not statistically significant. On the contrary, bleeding symptoms were statistically predominant in severe cases.

Table 1. Baseline Characteristics of the Study Population (n = 97)

Variable	Value
Age (years), mean ± SD	49.19 ± 19.10
Male, n (%)	47 (48.5)
Female, n (%)	50 (51.5)
Laboratory parameter	Median (IQR)
ALT (U/L)	193.0 (211.5)
AST (U/L)	344.0 (280.5)
Platelet count (×10 ⁹ /L)	107.0 (82.5)
Serum bilirubin (mg/dL)	2.09 (1.68)
Serum albumin (g/dL)	3.81 (0.72)

Likewise, hypotension and hepatomegaly were statistically more prevalent in the severe group than in non-severe patients. Table 2

Table 2. Comparison between Severe and Non-Severe Dengue Hepatitis (n = 97)

Variable	Non-severe (n = 62)	Severe (n = 35)	p-value
Platelet count, median (IQR)	109 (90.5)	96 (80.0)	0.583†
Bleeding, n (%)	6 (9.7)	18 (51.4)	<0.001‡
Hypotension, n (%)	6 (9.7)	12 (34.3)	0.003‡
Hepatomegaly, n (%)	6 (9.7)	12 (34.3)	0.003‡
ALT (U/L), median (IQR)	196.0 (208.3)	178.0 (201.0)	0.526†
AST (U/L), median (IQR)	344.0 (263.3)	344.0 (275.0)	0.555†
Serum bilirubin (mg/dL), median (IQR)	1.98 (1.65)	2.22 (1.60)	0.406†
Serum albumin (g/dL), median (IQR)	3.81 (0.73)	3.84 (0.73)	0.608†

† Mann-Whitney U test used for continuous variables, ‡ Chi-square test used for categorical variables. A p-value < 0.05 was statistically significant.

The multivariate logistic regression analysis was conducted to detect the independent predictors of severe dengue hepatitis. The complete model was statistically significant (Omnibus $\chi^2 = 39.30, p < 0.001$) and had good explanatory power with the Nagelkerke R² being 0.457, showing that the included variables accounted for about 46% of the variation in the severity of the disease. The model calibration was good based on an insignificant Hosmer-Lemeshow test (p = 0.550), which implied that it was in agreement with the observed and the predicted results (Table 3).

ROC curve analysis was conducted in order to find out the discriminative capacity of the individual clinical predictors in relation to severe dengue hepatitis. Bleeding had the greatest diagnostic accuracy with a good discriminatory performance. Hypotension and hepatomegaly were found to have a fair predictive value. These results substantiate the fact that these variables should be added to the dengue hepatitis severity scoring system (Table 4).

The dengue hepatitis severity score had a good discriminating power. An optimal balance between sensitivity and specificity of predicting severe dengue hepatitis was given by a cut-off value of ≥1 (Table 5).

Table 3. Multivariate Logistic Regression Analysis for Severe Dengue Hepatitis (n = 97)

Variable	β coefficient	Adjusted Odds Ratio (AOR)	95% CI	p-value
Platelet count	-0.003	0.997	0.986–1.008	0.624
ALT	0.003	1.003	0.998–1.008	0.178
AST	-0.002	0.998	0.994–1.001	0.235
Bleeding	2.420	11.24	3.28–38.51	<0.001
Hypotension	1.945	6.99	1.73–28.25	0.006
Hepatomegaly	1.783	5.95	1.54–22.94	0.010

Table 4. ROC Analysis of Clinical Predictors for Severe Dengue Hepatitis (n = 97)

Variable	AUC (95% CI)	p-value	Interpretation
Bleeding	0.709 (0.594–0.824)	0.001	Good discrimination
Hypotension	0.623 (0.502–0.744)	0.045	Fair discrimination
Hepatomegaly	0.623 (0.502–0.744)	0.045	Fair discrimination

Table 5. Diagnostic Performance of the Dengue Hepatitis Severity Score (n = 97)

Cut-off value	Sensitivity (%)	Specificity (%)	AUC (95% CI)	p-value
≥ 1	77.1	71.0	0.761 (0.659–0.863)	<0.001

DISCUSSION

The present study developed and evaluated a novel PIMS-specific Dengue Hepatitis Severity Score using routinely available bedside clinical variables among hospitalized patients with dengue-associated hepatic involvement. This study identified bleeding manifestations, hypotension, and hepatomegaly as independent predictors of severe dengue hepatitis. The commonly measured laboratory parameters, including platelet count, AST, and ALT levels, were not independently associated with severe disease after multivariable adjustment in this study. A three-point severity score derived from these predictors demonstrated good discriminatory performance, with an AUC of 0.761, and a good sensitivity and specificity at a cutoff value of ≥ 1 . Collectively, these findings suggest that readily identifiable clinical features may provide an effective and pragmatic approach for early risk stratification of dengue patients with hepatic involvement, particularly in resource-constrained healthcare settings. Recent research has revealed that complications of dengue and increased bleeding and shock to be linked with abnormal liver functioning tests and hepatomegaly^{11,12}.

The mean age of around 49 years suggests that dengue-associated hepatic complications are not only seen in younger populations but are increasingly affecting the middle-aged and older adults. This is in line with recent regional studies, showing a shift toward greater disease burden among older individuals, who often have a higher risk of organ involvement and severe clinical outcomes^{13,14}. The close gender distribution observed of

our study indicates severe hepatic involvement occurring across both sexes almost equally. Liver involvement has increasingly been identified as a determinant of dengue infection severity. The median AST and ALT values observed in our cohort reveal significant hepatic injury, with higher AST levels than ALT levels, a finding frequently described in dengue hepatitis. Earlier studies have also reported that AST predominance shows hepatocellular damage as well as injury to skeletal and cardiac muscle tissues as a result of systemic inflammation and viral infection. Studies conducted in Pakistan, Columbia, Nepal, and other dengue-endemic countries have reported similar observations where higher AST levels were associated with more severe clinical picture and longer hospitalization. The current findings therefore reinforce the existing evidence that liver involvement represents a clinically relevant component of dengue pathophysiology¹⁵⁻¹⁷.

Platelet count was not significantly associated with severe dengue hepatitis even after multivariate adjustment although thrombocytopenia remained prevalent in our patients. Recent studies have also made similar observations and propose that platelet count is not a reliable discriminator of severity and must be combined with clinical features^{18,19}. Conversely, bleeding manifestations were found as the most robust independent predictor of severe disease in our model²⁰. This observation concurs with the current evidence showing that the manifestation of overt bleeding is a sign of progressive capillary leakage, coagulopathy, and approaching clinical worsening²¹.

Another predictor of severe dengue hepatitis in our cohort

was hypotension. Hypotension is a manifestation of depletion of intravascular volume and progressive shock, the main mechanisms in severe dengue. Previous study has attested to the fact that an early hypotension closely correlates with intensive care hospitalization and poor outcomes²². Hepatomegaly was also predictive of severity by itself, which confirms prior studies that liver enlargement is an indication of hepatic inflammation, congestion, and early dysfunction in relation to complicated disease^{14,16}.

The Dengue Hepatitis Severity Score had good discriminatory ability, with AUC = 0.761. A cut-off of ≥ 1 had balanced sensitivity and specificity, and it suggests that even a single high-risk feature can be followed a bit more closely. Our score has a performance that is similar to new-proposed models of dengue severity, most of which incorporate organ involvement and clinical instability to enhance pre-emptive reports^{17,18}. The major strengths of this study are that it uses real-world EMR data, a standardized definition of hepatic involvement, and internal validity with a strong statistical tool.

Notably, this score is based on bedside clinical variables, which is particularly appropriate where advanced biomarkers or imaging may not be easily accessible.

Limitation: The limitation of the current study is its retrospective, single-center study design, which may have compromised the generalizability of results. Multicenter prospective studies in different populations should be done in future to validate this score, along with assessment of its effects on clinical decisions and patient outcomes.

CONCLUSION

This study successfully developed and evaluated a simple, three-point PIMS-specific Dengue Hepatitis Severity Score based on bleeding, hypotension, and hepatomegaly. The score had good discriminatory ability for predicting severe dengue hepatitis. With its reliance on easily available bedside clinical parameters, this score is practical and applicable in resource-limited settings. Early use of this scoring system can facilitate timely risk stratification, improve monitoring strategies, and support early clinical decision-making in dengue-associated hepatic involvement. However, external validation in larger, multicenter prospective cohorts is required prior to its routine implementation.

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AUTHORS' CONTRIBUTION

- Shaista Faheem:** Conception and design, Drafting the article, Critical revision.
- Sana Waqar:** Conception and design, Acquisition of data, Aanalysis and interpretation of data, Drafting the article, Critical revision.
- Fareha Rasheed:** Conception and design, Acquisition of data, Aanalysis and interpretation of data, Drafting the article.
- Maria Zafar:** Acquisition of data, Aanalysis and interpretation of data, Drafting the article, Critical revision.
- Samina Rashid:** Aanalysis and interpretation of data, Drafting the article.
- Aashar Khalid:** Conception and design, Acquisition of data, Drafting the article.

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