

Development and Validation of an Admission Risk Model for Intensive Care Unit Admission in Adults with Dengue: A Retrospective Cohort Study

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ABSTRACT

Introduction: Dengue outbreaks can place a major burden on hospitals, especially in countries such as India, where early triage is important in resource-limited settings. The novelty of this study lies in using routinely available admission variables to predict Intensive Care Unit (ICU) admission, a practical triage endpoint less studied than World Health Organisation (WHO)-defined severe dengue or mortality.

Aim: To develop and validate an admission-based risk model for predicting ICU admission in adults with laboratory-confirmed dengue.

Materials and Methods: A retrospective cohort study was conducted at a tertiary care teaching hospital in Belagavi, Karnataka, India, from April 2024 to March 2025. A total of 102 adults with fever, thrombocytopenia, and laboratory-confirmed dengue were included. The primary outcome was ICU admission during the same hospitalisation. Five admission-time predictors were evaluated: age, warning or severe signs, haematocrit, platelet count, and serum Aspartate aminotransferase (AST). Ridge-penalised multivariable logistic regression was used for model development. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 29.0 and a custom Python-based script. A p-value <0.05 was considered statistically significant. Internal validation was

performed using 1000 bootstrap resamples. Temporal external validation was conducted using an earlier cohort from the same hospital comprising 146 complete cases collected between September 2022 and September 2023.

Results: Of 102 adults with laboratory-confirmed dengue, 50 (49%) required ICU admission. These patients more frequently had warning or severe signs, older age, lower platelet counts, and higher AST levels. Univariable analyses demonstrated associations for age, warning/severe signs, and platelet count with ICU admission; haematocrit and AST were not independently associated. The final five-variable model demonstrated moderate discrimination in the development cohort (AUC 0.766; Brier score 0.203). Bootstrap internal validation yielded an optimism-corrected AUC of 0.687; In the temporal validation cohort, the model demonstrated an AUC of 0.676 and a Brier score of 0.209, with reduced calibration performance compared with the development dataset.

Conclusion: This five-variable admission model, based on routine clinical and laboratory parameters, demonstrated moderate performance to predict ICU admission in adults with dengue. It may support early risk assessment and triage during outbreaks, especially in resource-constrained settings, although further external validation and recalibration are required before routine clinical implementation.

Keywords: Haemorrhagic fever, Logistic models, Risk assessment, Severity of illness index, Triage, Viral

INTRODUCTION

Dengue fever remains a major clinical and public health problem in tropical and subtropical regions, where periodic outbreaks place considerable pressure on healthcare systems [1]. While most patients have a self-limited febrile illness, some progress to severe disease with plasma leakage, bleeding, organ involvement, or haemodynamic compromise. Early identification of patients at risk of clinical deterioration is important for improving outcomes and avoiding unnecessary escalation of treatment [2]. In 2024, a record 14.6 million dengue cases and 12,000 deaths were reported worldwide [3], of which India accounted for an estimated 230,000 dengue infections and 297 deaths [4].

The 2009 WHO classification grouped dengue into dengue without warning signs, dengue with warning signs, and severe dengue, providing a practical framework for monitoring and escalation of care [5]. Early triage is especially important in dengue. Unnecessary admissions can strain limited resources, while failure to identify high-risk patients may delay critical interventions [6]. In routine practice, however, admission decisions often depend on clinical judgment rather than an objective risk tool. Clinicians must decide whether a patient

needs care in a general ward, a high-dependency unit, or an ICU before overt deterioration occurs [6].

Several prediction models have been developed to identify patients at risk of severe dengue outcomes. During the 2015 dengue outbreak in Taiwan, Huang SW et al., used demographic and laboratory variables obtained at presentation to predict severe dengue and reported good discriminatory performance, with Area Under the receiver operating characteristic Curve (AUC) values approaching 0.85. Age, thrombocytopenia, and liver enzyme abnormalities emerged as important predictors of disease severity [7]. In another study from Taiwan, Kuo CY et al., applied feature-selection techniques and random forest algorithms to improve dengue prediction and identified several key variables that contributed to model performance, highlighting the potential value of routinely available clinical data for risk assessment [8].

Despite these encouraging results, most published models have focused on WHO-defined severe dengue, mortality, or composite complications rather than the practical question of which patients admitted with dengue may subsequently require ICU care. Therefore, there remains a need for a simple admission-based model that uses

routinely available clinical and laboratory variables to identify adults with dengue who are at increased risk of requiring intensive care during hospitalisation.

Thus, this study aimed to develop and internally validate a simple admission risk model to predict ICU admission in adults with fever, thrombocytopenia, and laboratory-confirmed dengue. The model used five routine admission variables: age, warning or severe signs, haematocrit, platelet count, and serum AST. The present study focused on calibration and bootstrap-based internal validation to improve transparency and facilitate future validation studies.

MATERIALS AND METHODS

This retrospective cohort study was conducted at KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, a tertiary care teaching hospital, in technical collaboration with the Department of Medical Microbiology, Jawaharlal Nehru Medical College, Belagavi, Karnataka, India and Zeuron.ai. The study included adult patients admitted between 1st April 2024 and 31st March 2025 with a history of fever, thrombocytopenia, and laboratory-confirmed dengue infection. The study was designed and reported in accordance with the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidelines [9]. Ethical approval was obtained from the Jawaharlal Nehru Medical College, Belagavi Institutional Ethical Committee, Belagavi (IEC No.: MDC/JNMC/IEC/55).

Inclusion criteria: Adults aged 18 years or older admitted with a history of fever, platelet count <150,000/ μ L, and laboratory-confirmed dengue infection were included in the study. Laboratory confirmation was defined as a positive NS1 antigen test and/or dengue IgM ELISA at admission.

Exclusion criteria: Patients younger than 18 years, pregnant, or had incomplete admission data for the prespecified predictor variables were excluded from the study.

Sample size: The sample size was calculated after discussion with the statistician. Based on the expected sensitivity, specificity, allowable error, and expected outcome proportion, the required sample size was about 102 patients [Appendix].

Study Procedure

A total of 102 adults with a history of fever, thrombocytopenia, and laboratory-confirmed dengue were included in the final development cohort. The sample size was determined by the number of eligible patients with complete data available during the study period. Among these patients, 50 required ICU admission. With five prespecified predictors included in the model, this corresponded to 10 outcome events per predictor (50/5 = 10).

Predictor variables were prespecified before model development based on clinical plausibility, pathophysiological relevance, and routine availability at the time of hospital admission. The following five predictors were selected:

1. Age (years), analysed as a continuous variable;
2. Presence of warning signs or severe signs at admission (binary: yes/no);
3. Admission haematocrit (%), analysed as a continuous variable;
4. Admission platelet count (cells/ μ L), analysed as a continuous variable;
5. Admission serum AST level (U/L), analysed as a continuous variable.

Continuous predictors were retained in their continuous form during model development to avoid loss of prognostic information associated with arbitrary categorisation.

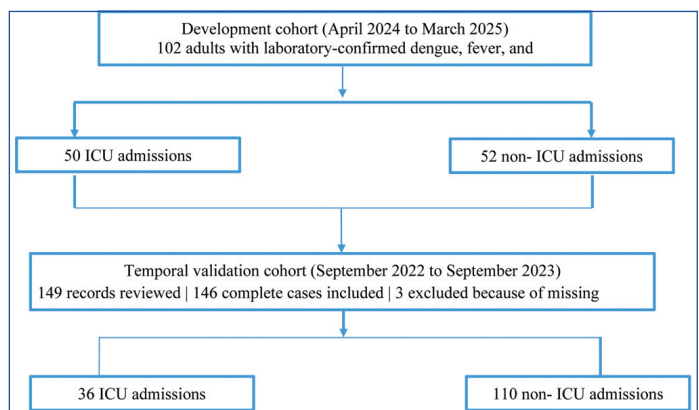
The primary outcome predicted by the multivariable model was ICU admission during hospitalisation in adults with laboratory-

confirmed dengue. This outcome was assessed retrospectively from inpatient medical records and recorded as a binary endpoint (ICU admission vs non-ICU admission) for each included patient. Decisions regarding ICU admission were made by the treating clinical team based on the patient's clinical condition, institutional protocols, and WHO 2009 dengue severity guidelines. Since ICU admission was decided by clinicians and not through a blinded protocol, some predictors in the model may also have influenced the ICU admission decision [5]. To make the model easier to use at the bedside, the locked model was also converted into a simple 0-15 score. For descriptive interpretation, total scores were categorised as low risk (0-4), moderate risk (5-9), and high risk (10-15) [Table/Fig-1].

Predictor	Category	Points	Predictor	Category	Points
Age (years)	<30	0	Platelet count (μ L)	\geq 100,000	0
	30-49	2		60,000-99,999	2
	\geq 50	4		20,000-59,999	3
Warning/ Severe signs	No	0	AST (U/L)	<20,000	4
	Yes	3		\leq 40	0
Haematocrit (%)	<40	0		41-1000	1
	40-44.9	1	>1000	2	
	\geq 45	2			

[Table/Fig-1]: Simplified 0-15 bedside risk score for prediction of ICU admission.

External validation was performed in a temporal cohort from the same hospital but from September 2022 to September 2023. This cohort included 146 complete cases, of which 36 required ICU admission [Table/Fig-2].



[Table/Fig-2]: Flow diagram of development and temporal validation cohorts.

STATISTICAL ANALYSIS

Data were entered in Microsoft Excel 2010. Statistical analysis was performed using SPSS version 29.0 and a custom Python-based script developed jointly by the authors.

A ridge-penalised multivariable logistic regression was utilised as the outcome was binary and the sample size was limited. A small set of clinically relevant predictors that are routinely available at admission was retained. Ridge penalisation was used to reduce overfitting and improve the stability of the model while keeping all prespecified predictors in the analysis. Continuous predictors were standardised before penalisation so that the penalty was applied evenly across variables measured on different scales. The tuning parameter was selected using internal cross-validation, and no automated variable selection was used. The final coefficients were also used to derive a simple additive risk score for easier bedside use as a secondary analysis.

Model performance was evaluated across three domains:

Discrimination assessed using the C-statistic (AUC) measures the model's ability to distinguish between patients who required ICU admission and those who did not. Calibration was assessed using calibration slope, calibration-in-the-large,

and visual inspection of calibration plots. Overall accuracy was assessed using the Brier score, which is a measure of overall prediction error, with lower values indicating better accuracy. Internal validation was performed using bootstrap resampling with 1,000 iterations. Bootstrap-based estimates were used to measure optimism in model performance and to calculate optimism-corrected performance values.

After developing the five-parameter ridge-penalised logistic regression model, a simplified 0-15 bedside risk score was also derived to improve clinical usability. Continuous predictors were grouped into clinically practical categories, and points were assigned according to the relative contribution of each predictor in the model. The score was subsequently assessed in both the development dataset and the temporal external validation cohort. The regression model remained the primary analytical model, while the simplified score was intended to support bedside interpretation. Associations between categorical variables were assessed using the Pearson chi-square test. A p-value <0.05 was considered statistically significant.

RESULTS

The development cohort included 102 patients. Of these, 50 (49.0%) required ICU admission. Warning or severe signs at admission were present in 67 patients in total (65.7%). The median age of the cohort was 35.0 years (Interquartile Range (IQR) 24.0-51.5). The median admission platelet count was 58,500/ μ L (IQR 22,000-109,000), median haematocrit was 43.2% (IQR 37.0-49.4), and median serum SGOT (AST) was 108.0 U/L (IQR 56.0-180.3). Patients who required ICU admission were older and had lower platelet counts and higher AST values than those who did not. Haematocrit values were similar between the two groups [Table/Fig-3].

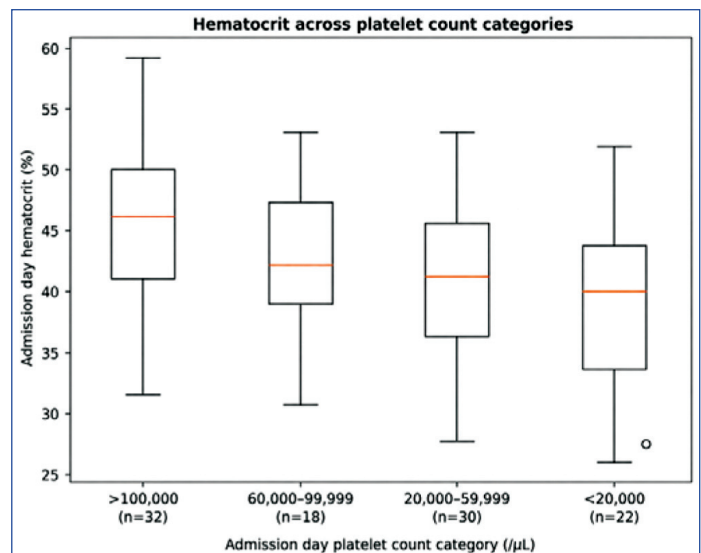
Variable	Overall (n=102)	ICU (n=50)	Non ICU (n=52)
Age group (years), n (%)			
<30	40 (39.2)	16 (40.0)	24 (60)
30-49	36 (35.3)	15 (41.7)	21 (58.3)
\geq 50	26 (25.5)	19 (73)	7 (27)
Warning/severe signs present, n (%)			
Warning/severe signs present, n (%)	67 (65.7)	40 (59.7)	27 (40.3)
No warning/severe signs present, n (%)			
No warning/severe signs present, n (%)	35 (34.3)	10 (28.6)	25 (71.4)
Platelet count category (μL), n (%)			
>100,000	32 (31.4)	12 (37.5)	20 (62.5)
60,000-99,999	18 (17.6)	4 (22.2)	14 (77.8)
20,000-59,999	30 (29.4)	19 (63.3)	11 (36.7)
<20,000	22 (21.6)	15 (71.4)	7 (28.6)
AST category, (U/L) n (%)			
\leq 40	15 (14.7)	5 (33.3)	10 (66.7)
41-1000	80 (78.4)	40 (50)	40 (50)
>1000	7 (6.9)	5 (71.4)	2 (28.6)
Haematocrit, (%) n (%)			
<40	34 (33.3)	16 (47.1)	18 (52.9)
40-44.9	27 (26.5)	13 (48.1)	14 (51.9)
\geq 45	41 (40.2)	21 (51.2)	20 (48.8)

[Table/Fig-3]: Distribution of predictor categories by ICU admission status.

+Percentages in ICU and non-ICU columns are row percentages within each predictor category

The final model included five prespecified predictors, with an Events-Per-Predictor (EPP) ratio of 10.0.

Although lower platelet categories showed a modest tendency toward higher haematocrit values, considerable overlap in haematocrit distributions was observed across groups. The displayed outlier within the <20,000/ μ L category represents a haematocrit value within that subgroup [Table/Fig-4]. Older age, presence of warning or severe signs at admission, and lower platelet



[Table/Fig-4]: Distribution of admission haematocrit across platelet count categories.

count were associated with ICU admission in univariable analysis. Haematocrit and AST were not significantly associated with ICU admission in univariable analysis [Table/Fig-5].

Predictor	Unadjusted OR (95% CI)	Exact p-value
Age (per 10-year increase)	1.40 (1.09-1.79)	0.0088
Warning or severe signs at admission (yes vs no)	4.86 (1.92-12.34)	0.0009
Haematocrit (per 5% increase)	0.97 (0.75-1.26)	0.8105
Platelet count (per 10,000/ μ L decrease)	1.17 (1.07-1.27)	0.0006
AST (per 50 U/L increase)	1.01 (0.99-1.03)	0.4180

[Table/Fig-5]: Univariable association of candidate predictors with ICU admission.

The ridge-penalised multivariable model retained all five prespecified predictors, although the strength of association varied after penalisation. Older age, presence of warning or severe signs, and lower platelet counts contributed more strongly to predicted ICU admission risk, whereas haematocrit and AST demonstrated comparatively smaller contributions within the multivariable framework [Table/Fig-6].

Predictor	Beta	Interpretation
Intercept	-0.1119	Baseline log-odds
Age	0.01835	Risk increases with age
Warning or severe signs	0.3690	Positive contributor
Haematocrit	-0.00785	Small inverse adjusted effect
Platelet count	-0.00000826	Lower platelets increase risk
AST	0.0000429	Small positive adjusted contribution

[Table/Fig-6]: Final model coefficients and interpretation.

How to use this model for an individual patient; To estimate the probability of ICU admission for an individual patient, enter the patient's values into the following equation:
 $\text{logit}(p) = -0.1119 + 0.01835(\text{Age}) + 0.3690(\text{WS}) - 0.00785(\text{Haematocrit}) - 0.00000826(\text{Platelet count}) + 0.0000429(\text{AST})$; where WS = 1 if warning or severe signs are present and WS = 0 if warning or severe signs are absent. The probability is then calculated as: $p = 1 / (1 + e^{-\text{logit}(p)})$

In the development cohort, the model showed moderate discrimination, with an AUC of 0.766 and a Brier score of 0.203. The calibration intercept+ was 0.003, and the calibration slope++ was 1.827 [Table/Fig-7]. This suggests that, in the development cohort, the model may have underestimated the difference between lower-risk and higher-risk patients.

Internal validation was performed using 1000 bootstrap resamples. The optimism-corrected AUC was 0.687, and the optimism-corrected Brier score was 0.238 [Table/Fig-7]. Internal validation showed only a small optimism-corrected reduction in discrimination, indicating limited optimism in the apparent AUC. However, the calibration slope was greater than 1, which does not suggest overfitting; rather, it indicates that predicted risks may have been

Metric	Apparent performance	Optimism-corrected performance
AUC	0.766	0.687
Brier score	0.203	0.238
Calibration intercept	0.003	-0.004
Calibration slope	1.827	1.496

[Table/Fig-7]: Apparent and optimism-corrected performance of the final model after bootstrap internal validation (1000 resamples).
 + Calibration intercept: Indicates whether predicted risks are systematically too high or too low overall; ++ Calibration slope: Indicates agreement between predicted and observed risks; values close to 1 indicate better calibration

insufficiently extreme, consistent with mild underfitting or under-calibration.

At the default probability threshold of 0.50, sensitivity was 78.0%, specificity was 65.4%, Positive Predictive Value (PPV) was 68.4%, Negative Predictive Value (NPV) was 75.6%, and accuracy was 71.6%. At the Youden-optimal threshold of 0.483, sensitivity increased to 80.0%, while specificity remained 65.4%. At this threshold, PPV was 69.0%, NPV was 77.3%, and accuracy was 72.5% [Table/Fig-8].

Measure	0.50 threshold	0.483 threshold
Sensitivity	78.0%	80.0%
Specificity	65.4%	65.4%
PPV	68.4%	69.0%
NPV	75.6%	77.3%
Accuracy	71.6%	72.5%
TP	39	40
FP	18	18
FN	11	10
TN	34	34

[Table/Fig-8]: Classification performance of the final model at the 0.50 and Youden-optimal (0.483) probability thresholds.
 • PPV: Positive predictive value; proportion of predicted ICU admissions that were true ICU admissions;
 • NPV: Negative predictive value; proportion of predicted non-ICU cases that were truly non-ICU;
 • TP: True positive; patient correctly classified as requiring ICU admission;
 • FP: False positive; patient incorrectly classified as requiring ICU admission;
 • FN: False negative; patient incorrectly classified as not requiring ICU admission;
 • TN: True negative; patient correctly classified as not requiring ICU admission

External Validation

Of the 149 records reviewed, 146 complete cases were available for analysis, including 36 ICU admissions and 110 non ICU admissions. Three patients had missing data for warning/severe signs, one of whom also had a missing admission platelet count. Accordingly, three patients were excluded from the final multivariable analysis. In this cohort, the model showed an AUC of 0.676 and a Brier score of 0.209. The calibration intercept was -0.943, and the calibration slope was 0.722 [Table/Fig-9]. This suggests that, in the temporal validation cohort, the model may have overestimated risk differences

Metric	Value
Total records reviewed	149
Complete cases included	146
Missing warning or severe-sign coding only	2
Missing warning or severe-sign coding and platelet count	1
Total excluded due to missing predictor data	3*
AUC	0.676
Brier score	0.209
Calibration intercept	-0.943
Calibration slope	0.722

[Table/Fig-9]: Temporal external validation cohort and model performance.
 *Three patients were excluded because of missing predictor data. Two patients had missing documentation of warning/severe signs only, while one additional patient had both missing warn-ing/severe-sign documentation and a missing admission platelet count

between patients. This difference from the development cohort may be due to variations in patient profile, ICU admission practices, or documentation between the two time periods. Therefore, recalibration may be needed before applying the model to other cohorts.

At the default threshold of 0.50, sensitivity was 61.1%, specificity was 66.4%, PPV was 37.3%, NPV was 83.9%, and accuracy was 65.1%. At the model-specific threshold of 0.483, sensitivity increased to 69.4%, while specificity was 62.7%. PPV was 37.9%, NPV was 86.3%, and accuracy was 64.4%. Overall, the model retained moderate discrimination in the temporal validation cohort, although calibration was less satisfactory than in the development dataset [Table/Fig-10].

Measure	0.50 threshold	0.483 threshold
Sensitivity	61.1%	69.4%
Specificity	66.4%	62.7%
PPV	37.3%	37.9%
NPV	83.9%	86.3%
Accuracy	65.1%	64.4%
TP	22	25
FP	37	41
FN	14	11
TN	73	69

[Table/Fig-10]: Classification performance of the final model in the temporal external validation cohort at the 0.50 and 0.483 probability thresholds.

DISCUSSION

The major strength of this study was its focus on a practical clinical question faced during dengue outbreaks: identifying, at admission, which patients are more likely to require ICU care later in their hospital stay. This early triage perspective is clinically relevant, as timely recognition of high-risk patients can guide monitoring intensity and resource allocation. The model demonstrated moderate discriminative ability in both the development and temporal validation cohorts, though calibration was less satisfactory in the temporal validation cohort, underscoring the importance of external validation and recalibration before clinical use.

The present study findings align with the broader literature on dengue prognostic modelling. A systematic review by Díaz-Arocutipá C et al., highlighted that while many published models achieved acceptable discrimination, calibration was often inadequately reported and methodological quality varied, with high-risk of bias in several studies [10]. More recently, Sangkaew S et al., developed and validated prediction models in febrile children in Vietnam and Thailand, achieving AUC values above 0.80 for progression to WHO-defined severe dengue [11]. Similarly, Madewell ZJ et al., applied machine-learning approaches to laboratory-confirmed dengue cases in Puerto Rico, with gradient boosting algorithms achieving excellent discrimination (CatBoost AUC-ROC 0.971). Key predictors included haemoconcentration, leukopenia, and timing of presentation, and performance remained high even when laboratory variables were excluded, reflecting adaptability to resource-limited settings [12].

In the present study cohort, older age, the presence of warning or severe signs, and lower platelet counts were strongly associated with ICU admission. These results are consistent with prior studies identifying thrombocytopenia, warning signs, and markers of clinical deterioration as predictors of severe outcomes [13-15]. In contrast, haematocrit and AST contributed less to risk prediction. Although widely used in dengue assessment, their predictive value may vary depending on illness stage and timing of laboratory testing, which may explain their weaker association in our dataset.

Another strength of the present study was the use of a small number of routinely available admission variables, enhancing applicability in real-world outbreak settings where rapid triage decisions are required. Predictors were prespecified before model development, reducing

the risk of data-driven selection bias. Methodologically, ridge-penalised logistic regression improved model stability in a modest-sized dataset, and performance was assessed comprehensively using discrimination, calibration, bootstrap internal validation, and temporal external validation. This structured approach enhances transparency and reproducibility, addressing common limitations noted in prior prognostic research.

Limitation(s)

This study had several limitations. First, although the final cohort included 102 patients with 50 ICU admissions, the sample size was modest, and some uncertainty in model estimates remains. Second, the study was conducted at a single tertiary care centre using retrospective hospital records, which may limit generalisability. The findings depended on the completeness and accuracy of available clinical data, and ICU admission was chosen as the outcome because it reflects clinically important deterioration. However, ICU admission was not equivalent to WHO-defined severe dengue, and decisions may have been influenced by local practice patterns and resource availability.

Third, although the model was simplified into a 0-15 score, risk categories (low, intermediate, high) were not formally defined. The score should therefore not be used in isolation to guide ward versus ICU admission decisions. Finally, temporal validation was performed using an earlier cohort from the same hospital, which may not fully capture variability across different institutions or populations. Further multicentre studies with larger sample sizes are needed to evaluate the model's performance and calibration in diverse clinical settings.

CONCLUSION(S)

In adults admitted with laboratory-confirmed dengue, this five-variable admission model showed moderate ability to predict ICU admission. Because it uses routine admission variables and was also tested in a temporal validation cohort, it may be useful as an early risk-assessment tool. However, further validation is needed before routine clinical use.

Supplementary material is available as [\[Appendix\]](#).

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