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EVALUATING THE PREDICTIVE VALIDITY OF PLATELET COUNT, PLATELET-TO-LYMPHOCYTE RATIO, AND HEMATOCRIT FOR DENGUE SHOCK SYNDROME IN PEDIATRIC PATIENTS

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ABSTRACT

Background: *Dengue infection remains a major public health burden in tropical and subtropical regions, contributing significantly to pediatric hospitalizations, morbidity, and healthcare resource utilization. Early identification of patients at risk of developing dengue shock syndrome (DSS) is crucial to reduce complications and mortality. However, in resource-limited settings such as Vietnam, access to advanced diagnostic tools is often restricted, underscoring the need for simple, cost-effective, and widely available biomarkers. Despite growing interest in hematological indices, evidence on their predictive validity for DSS remains scarce and inconclusive, particularly in pediatric settings.* ***Objectives:*** *This study aimed to evaluate the prognostic value of platelet count, platelet-to-lymphocyte ratio (PLR), and hematocrit in predicting DSS in pediatric patients with dengue hemorrhagic fever (DHF), focusing on both predictive accuracy and model fit.* ***Materials and methods:*** *This analytical study included pediatric patients diagnosed with DHF at Can Tho Children's Hospital between December 2022 and February 2025. Eligible participants were followed from hospital admission until either DSS development or discharge. Demographic, clinical, and laboratory data, including complete blood count parameters, were collected. The discriminatory ability of platelet count, PLR, and hematocrit for predicting DSS was assessed using receiver operating characteristic (ROC) curve analysis. Calibration was evaluated using the Hosmer-Lemeshow test.* ***Results:*** *A total of 318 children were included, with 22% progressing to DSS. Platelet count, PLR, and hematocrit significantly differed between the DSS and non-DSS groups ($p<0.001$). Platelet count demonstrated the highest predictive performance (AUC=0.847, 95% CI: 0.8–0.894), followed by hematocrit (AUC=0.772, 95% CI: 0.7–0.844) and PLR (AUC=0.727, 95% CI: 0.657–0.797). Calibration analysis showed good agreement between predicted and observed DSS cases (platelet: $p=0.604$; PLR: $p=0.499$; hematocrit: $p=0.764$).* ***Conclusions:*** *Among the hematological parameters studied, platelet count exhibited the strongest predictive value for DSS. Given its accessibility in resource-limited settings, platelet count can serve as a practical marker for early DSS risk stratification in pediatric patients.*

Keywords*: dengue shock syndrome, platelet, platelet-to-lymphocyte ratio, hematocrit, pediatrics.*

I. INTRODUCTION

Dengue is the most common mosquito-borne viral disease globally, posing an increasing burden on public health, particularly in tropical regions. The circulation of all four serotypes from Asia to the Americas, Africa, and the Eastern Mediterranean raises concerns of a potential pandemic [1]. Over 70% of those at risk-around 1.8 billion people-

reside in the WHO South-East Asia and Western Pacific Regions, which account for nearly 75% of global cases [2]. Over the past five decades, dengue incidence has risen 30-fold, with an estimated 50-100 million infections annually across more than 100 endemic countries [1]. In most cases, while many infections are self-limiting, a subset progresses to severe disease. In children and young adults, Dengue Shock Syndrome (DSS) can occur around defervescence due to systemic vascular leak syndrome [3]. DSS, marked by plasma leakage and severe intravascular volume loss, may lead to hypoperfusion, metabolic acidosis, coagulopathy, and multiorgan failure if not promptly treated [2].

Laboratory markers like platelet count and hematocrit are routinely used to monitor dengue severity [2]. Low platelet counts and elevated hematocrit are independently linked to severe dengue in children [4]. Daily platelet monitoring is critical, as declining counts, especially the day before DSS onset, have been observed in affected patients [5]. Hemoconcentration (≥20% rise in hematocrit) indicates plasma leakage, with levels >41% associated with DSS in over 78% of cases [2],[6]. A 2024 study also reported decreased Platelet-to-Lymphocyte Ratios (PLR) in DHF and DSS, due to thrombocytopenia and relative lymphocytosis [7]. However, studies on PLR as a predictor of DSS in pediatric patients remain limited. Multiple studies have examined hematological predictors of DSS, yet applying complex models in resource-limited settings remains difficult [4],[5]. This study therefore evaluates the predictive utility of platelet count, hematocrit, and PLR for forecasting DSS in pediatric patients in Vietnam.

II. MATERIALS AND METHODS

2.1. Materials

All children aged 16 years or younger who were diagnosed with dengue hemorrhagic fever (DHF) and admitted to Can Tho Children's Hospital during the study period (from December 2022 to February 2025) were eligible for inclusion.

- **Inclusion criteria:** (i) Diagnosis of dengue virus infection confirmed by a positive NS1 test and/or a positive IgM serology test or ELISA. (ii) Classified as having DHF with or without warning signs, based on the criteria established in Decision No. 3705/QĐ-BYT, issued by the Ministry of Health on August 22, 2019 [8].

- **Exclusion criteria:** (i) Children with comorbid conditions such as liver failure, renal failure, hematologic disorders, congenital heart disease, or nephrotic syndrome. (ii) Children receiving medications that may affect the coagulation process. (iii) Children who did not undergo the necessary laboratory tests within 24 hours of hospital admission or had these tests performed only after the outcome occurred.

2.2. Methods

- **Study design and sampling method:** An ambispective cohort study was conducted using convenience sampling methods, and all eligible participants during the study period were included until the required sample size was reached.

- **Sample size:** The sample size was determined using the formula for hypothesis testing of a single proportion: $n = \frac{(Z_{\frac{\alpha}{2}}+Z_{\beta})^2 p(1-p)}{d^2}$; where, n: minimum required sample size; α: significance level, set at 0.05; β: Type II error, set at 0.2; Z: standard normal critical value, where $Z_{\frac{\alpha}{2}}$=1.96 and Z_{β}=0.84; d: desired margin of error, set at 0.07; p: proportion of children progressing to DSS. Based on the study by Nguyen *et al.,* this proportion is 25% [9].

Adjusting for an estimated 6% attrition rate due to incomplete data, the minimum required sample size for this study is 318 children.

- **Data collection:** Demographic, clinical, and paraclinical data, including complete blood count (CBC) results, were collected at admission. Participants were followed until either DSS developed or discharge occurred (for non-DSS cases). DSS was diagnosed when all criteria for dengue hemorrhagic fever (DHF) are present, along with evidence of circulatory failure. This circulatory failure is indicated by a rapid and weak pulse and a narrow pulse pressure (≤20 mmHg), or by age-specific hypotension accompanied by cold, clammy skin, restlessness or lethargy, reduced urine output, and, in severe cases, unmeasurable blood pressure and undetectable pulse [8]. For retrospective data, the same approach was applied using medical records. If CBC testing was delayed at admission due to logistical constraints, results obtained within the first 24 hours were used. Clinical outcomes (DSS progression or not) were documented during hospitalization.

- **Statistical analysis:** All analyses were conducted using R version 4.4.2. Categorical variables were reported as frequency (percentage), and quantitative variables as mean ± standard deviation, with comparisons made using independent *t*-tests. ROC curve analysis was used to assess the discrimination of platelet count, PLR, and hematocrit, with results presented as AUC, 95% CI, and p-values. AUCs were compared using DeLong's test. Optimal cutoff points were determined via Youden's index. Calibration was evaluated using the Hosmer–Lemeshow test, reported with deciles of risk, $\chi^2(df)$, and p-value. A p-value <0.05 was considered statistically significant.

- **Ethical approval:** This study proposal was reviewed and approved under IRB No. 24.129.SV/PCT-HĐĐĐ, issued on November 09, 2024, by Ethics Committee in Biomedical Research at Can Tho University of Medicine and Pharmacy.

III. RESULTS

2.1. Characteristics of Study Participants

Table 1. General characteristics of patients

Characteristics		Frequency (%)
Age (years), mean ± SD		9.7 ± 4.1
Sex	Male	181 (56.9)
	Female	137 (43.1)
Nutritional status	Normal	223 (70.1)
	Overweight/obesity	67 (21.1)
	Underweight	28 (8.8)
Day of illness, median (IQR)		4 (2–4)
Admission diagnosis	DHF	244 (76.7)
	DHF with warning signs	74 (23.3)
Outcome	No Progression to DSS	248 (78.0)
	Progression to DSS	70 (22.0)

Note. SD: standard deviation; IQR: interquartile range; DHF: dengue hemorrhagic fever; DSS: dengue shock syndrome.

A total of 318 patients were included in the study during the study period. The median age of the children was 9.7±4.1 years. Most were diagnosed with DHF without warning signs. DSS progression occurred in 22% of cases (Table 1).

Compared to the non-DSS progression group, the DSS progression group had significantly lower platelet counts, lower PLR, and higher hematocrit levels (Table 2).

Table 2. Association of platelet count, platelet-to-lymphocyte ratio, and hematocrit with the outcome

	Total (n=318)	DSS Progression (n=70)	Non-DSS Progression (n=248)	OR (95% CI)	p-value*
Platelet (x10^3/mm^3)	129±86.2	57.3 ± 39.7	149 ± 85.1	0.05 (0.02–0.12)	<0.001
PLR	99.8±78.8	61.3 ± 55.4	111 ± 81.1	0.30 (0.18–0.5)	<0.001
Hematocrit (%)	40.6±4.5	44.2 ± 5.2	39.6 ± 3.7	4.35 (2.74–6.9)	<0.001

*Note. *p-values from both the t-test comparison and the multivariable logistic regression (adjusted for age, sex, and nutritional status). OR: odds ratio; CI: confidence intervals; PLR: platelet-to-lymphocyte ratio.*

2.2. Discriminatory ability of platelet count, platelet-to-lymphocyte ratio, and hematocrit in predicting dengue shock syndrome

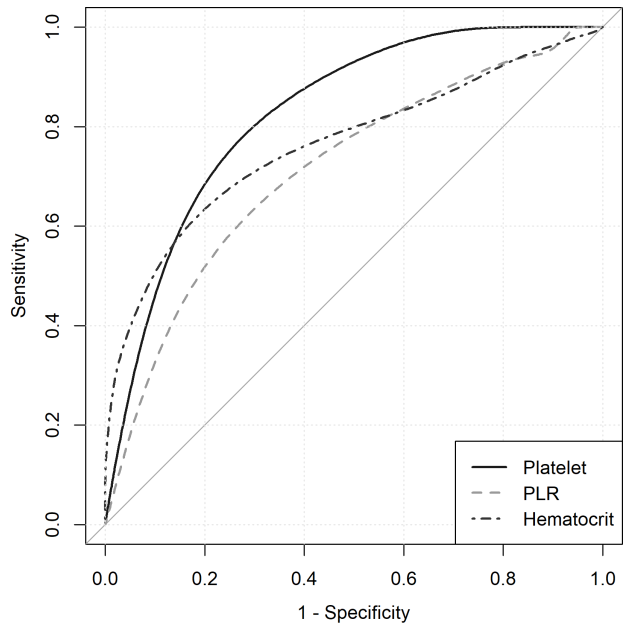

Figure 1. Receiver operating characteristic curves of platelet count, platelet-to-lymphocyte ratio, and hematocrit in discriminating dengue shock syndrome.

Figure 1 illustrates that the overall AUC for PLR was 0.727 (95% CI: 0.657–0.797, p<0.001), indicating moderate discriminatory ability. The hematocrit showed an AUC of 0.772 (95% CI: 0.7–0.844, p<0.001). For the platelet, the overall AUC of 0.847 (95% CI: 0.8–0.894, p<0.001) which was higher than AUC of the other two hematological parameters, suggesting better discrimination in predicting DSS.

The DeLong test revealed significant differences when comparing platelet with PLR and platelet with hematocrit (p<0.001, and p=0.049, respectively). However, no significant difference was observed between hematocrit and PLR (p=0.285). These findings indicate that platelet is the most effective index for predicting DSS.

Table 3. Prognostic performance of platelet count, platelet-to-lymphocyte ratio, and hematocrit for predicting dengue shock syndrome

	Platelet ($x10^3/mm^3$)	Platelet-to-Lymphocyte Ratio	Hematocrit (%)
AUC	0.847 (0.8 – 0.894)	0.727 (0.657 – 0.797)	0.772 (0.7 – 0.844)
Optimal cut-off	≤80	≤46	≥42
ACC (%)	78.6 (78.5 – 78.7)	76.1 (76.0 – 76.2)	74.2 (74.1 – 74.3)
Se (%)	77.1 (67.3 – 87.0)	55.7 (44.1 – 67.4)	72.9 (62.4 – 83.3)
Sp (%)	79.0 (74.0 – 84.1)	81.9 (77.1 – 86.7)	74.6 (69.2 – 80.0)
PPV (%)	50.9 (41.4 – 60.5)	46.4 (35.8 – 57.1)	44.7 (35.6 – 53.9)
NPV (%)	92.5 (88.9 – 96.0)	86.8 (82.4 – 91.1)	90.7 (86.7 – 94.7)
PLR	3.68 (2.8 – 4.84)	3.07 (2.19 – 4.30)	2.87 (2.22 – 3.71)
NLR	0.29 (0.19 – 0.45)	0.54 (0.41 – 0.71)	0.36 (0.25 – 0.54)

Note. Data are presented as values and their 95% confidence intervals. AUC: area under the curve; ACC: accuracy; Se: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value; PLR: positive likelihood ratio; NLR: negative likelihood ratio.

Using the Youden index, the optimal cutoff values for platelet count, platelet-to-lymphocyte ratio (PLR), and hematocrit to predict DSS were ≤80x10^3/ mm^3, ≤46, and ≥42%, respectively (Table 3). Among these parameters, platelet count had the highest sensitivity at 77.1%, while PLR had the highest specificity at 81.9%. The positive likelihood ratios for platelet count, PLR, and hematocrit were 3.68, 3.07, and 2.87, respectively.

2.3. Calibration ability of platelet count, platelet-to-lymphocyte ratio, and hematocrit in predicting dengue shock syndrome

The Hosmer-Lemeshow test was used to assess the calibration of the models across deciles of shock progression risk, as shown in Table 4. No statistically significant differences were found between the observed and predicted DSS rates for any of the parameters (platelet: p=0.604; PLR: p=0.499; hematocrit: p=0.764).

Table 4. Hosmer-Lemeshow test for deciles of risk based on platelet count, platelet-to-lymphocyte ratio, and hematocrit in predicting dengue shock syndrome

Platelet			PLR			Hematocrit		
Prob	O	E	Prob	O	E	Prob	O	E
0.046-0.047	0	1.5	0.045-0.064	4	1.7	0.053-0.064	3	1.9
0.047-0.051	0	1.6	0.064-0.089	2	2.6	0.064-0.077	4	2.3
0.051-0.057	1	1.8	0.089-0.114	5	3.3	0.077-0.087	4	2.8
0.057-0.073	3	2.2	0.114-0.147	2	3.9	0.087-0.110	2	3.1
0.073-0.098	3	2.6	0.147-0.177	5	5.2	0.110-0.138	2	3.5
0.098-0.154	6	3.8	0.177-0.218	6	6.2	0.138-0.173	4	4.9
0.154-0.253	8	6.3	0.218-0.286	6	7.7	0.173-0.229	6	6.7
0.253-0.446	11	11.4	0.286-0.362	8	10.3	0.229-0.317	8	9.0
0.446-0.624	17	16.3	0.362-0.448	15	12.8	0.317-0.526	11	11.8
0.624-0.801	21	22.6	0.448-0.554	17	16.1	0.526-0.948	26	24.0
$\chi^2(df)$=6.38(8), p=0.604			$\chi^2(df)$=7.36(8), p=0.499			$\chi^2(df)$=4.94(8), p=0.764		

Note. Prob: probability range; O: observed DSS value; E: expected DSS value; DSS: dengue shock syndrome; PLR: platelet-to-lymphocyte ratio.

IV. DISCUSSION

4.1. General characteristics

The DSS rate in our study was 22%, exceeding previously reported rates in both Vietnam and internationally [5],[10]. This difference may be due to our focus on confirmed dengue cases, whereas other studies included all suspected dengue admissions. The indices we studied were collected at the time of admission, although patients were included regardless of their day of illness. The median day of illness at admission was 4 (IQR: 2–4), suggesting that these parameters may have greater predictive value around day 4 of illness, when significant clinical and laboratory changes typically occur. In the comparison of platelet count, PLR, and hematocrit between outcome groups, significant thrombocytopenia was noted in the DSS progression group, with a platelet count of 57.3 ± 39.7 $x10^3/mm^3$. This value was lower than that reported in a study conducted at the Hospital for Tropical Diseases in Ho Chi Minh City, where the median platelet count was 100,000 (IQR: 80,000–150,000) [5]. The platelet count in the non-DSS progression group remained at 149 ± 85.1 $x10^3/mm^3$, comparable to that reported in a 2017 study [5]. Hematocrit levels were also higher in the DSS group (44.2 ± 5.2%), approximately 6% above those in the non-DSS group, and surpassing the levels reported by Tran *et al.* [10]. To our knowledge, pediatric studies evaluating PLR as a predictor of DSS are lacking. A 2024 study by Böer *et al.* examined PLR in adult dengue patients, its prognostic value in pediatric DSS remains unclear [11].

4.2. Discrimination

In our study, platelet count showed excellent discriminatory power for predicting DSS, with an AUC of 0.847 (95% CI: 0.800–0.894). Thrombocytopenia has been widely studied as a marker of dengue severity. Lam *et al.* reported a lower AUC of 0.68 on day 3 of illness in a cohort of 2,301 pediatric patients, indicating weaker predictive value compared to our findings [5]. Hematocrit, reflecting hemoconcentration due to plasma leakage, showed moderate discrimination with an AUC of 0.772 (95% CI: 0.700–0.844, $p<0.001$), also exceeding the 0.68 reported by Lam *et al.* [5]. This difference may relate to our exclusive inclusion of DHF patients, whereas Lam *et al.* included both DF and DHF cases [5]. PLR demonstrated moderate predictive ability, with an AUC of 0.727 (95% CI: 0.657–0.797). DeLong test comparisons showed significant differences between platelet vs. PLR and platelet vs. hematocrit, but not between hematocrit and PLR, indicating platelet count as the strongest individual predictor of DSS.

A platelet count ≤80 $x10^3/mm^3$ showed the best diagnostic performance for predicting DSS, with an accuracy of 78.6%, sensitivity of 77.1%, and specificity of 79%. The PPV was 50.9%, while the NPV was high at 92.5%, indicating strong utility in ruling out DSS in patients with normal counts. For PLR, the optimal cutoff was ≤46, yielding 55.7% sensitivity and 81.9% specificity. While its PPV was modest (46.4%), the NPV of 86.8% suggests it is useful for excluding DSS in low-risk cases. Hematocrit ≥42%, demonstrated moderate diagnostic value, with 74.2% accuracy, 72.9% sensitivity, and 74.6% specificity. Although its PPV was 44.7%, the NPV of 90.7% supports its role in excluding DSS when below threshold. As shown in Table 3, platelet count offered the best overall balance of sensitivity and specificity. Its low negative likelihood ratio further enhances its utility. Hematocrit had the lowest accuracy, underscoring the benefit of using multiple parameters in combination for improved DSS prediction.

4.3. Calibration

In assessing the calibration of DSS predictions in children with DHF, all three parameters (platelet count, PLR, and hematocrit) demonstrated good calibration. The reliability of these models in predicting DSS was supported by their Hosmer-Lemeshow test p-values: 0.604 for platelet count, 0.499 for PLR, and 0.764 for hematocrit, indicating no significant differences between the predicted and observed DSS cases. Therefore, these three parameters are considered reliable for DSS prediction in children with DHF, as they show a good alignment between expected and actual outcomes.

V. CONCLUSION

This study showed that platelet count, PLR, and hematocrit are valuable prognostic markers of DSS in children with DHF, with platelet count demonstrating the superior sensitivity and predictive accuracy. In resource-limited pediatric settings, such as in Vietnam, platelet count represents a practical, low-cost biomarker due to its routine availability through standard blood tests. Its strong performance in both discrimination and calibration supports its role in early DSS risk assessment. Further studies are needed to validate these markers across diverse clinical settings and to support their inclusion in pediatric dengue risk stratification protocols.

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