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Predicting septic shock and mortality in pediatric sepsis using CBC indices with and without immature granulocyte: a prospective study

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Abstract

Background Pediatric sepsis is a major cause of mortality in low- and middle-income countries (LMICs), where affordable prognostic tools are needed. This study aimed to evaluate whether a panel of complete blood count (CBC) indices - hemoglobin (Hb), lymphocyte count, and platelet count - used jointly in logistic regression, with or without immature granulocyte (IG) percentage, predicts septic shock and in-hospital mortality in children with sepsis.

Methods In this prospective study at a Tertiary Pediatric Centre (July 2023–July 2025), 276 children with sepsis (1 month–16 years) were enrolled. CBC indices were measured in all patients; immature granulocytes counts were available in a subgroup ($n=52$). Logistic regression with propensity score weighting assessed prediction of septic shock and mortality using area under the receiver operating characteristic curve (AUC), net reclassification improvement (NRI), integrated discrimination improvement (IDI), and decision curve analysis.

Results The CBC panel model (Hb, lymphocyte count, platelet count) predicted septic shock (AUC 0.725) and mortality (AUC 0.746). Adding immature granulocytes improved AUCs in the subgroup (0.908 and 0.807), but NRI, IDI, and decision curves indicated limited incremental benefit.

Conclusions CBC indices provide moderate-to-good prognostic accuracy in pediatric sepsis and remain practical in LMICs. IG offers slight improvement but limited feasibility.

Keywords Pediatric sepsis, Complete blood count, Immature granulocytes, Prognostic model, Low- and middle-income countries

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Background

Pediatric sepsis is a major cause of preventable mortality and morbidity, responsible for an estimated 2.9 million deaths annually in children under five and nearly half of all global sepsis cases [1, 2]. Mortality rates range from 3 to 7% in general pediatric sepsis to more than 20% in septic shock, and can exceed 50% in some low- and middle-income countries (LMICs) [3]. Despite the high burden, prognostic models for pediatric sepsis remain limited, particularly in resource-constrained settings, where advanced laboratory and imaging modalities may not be available [4, 5]. This creates an urgent need for prognostic tools that are rapid, cost-effective, and universally accessible.

The complete blood count (CBC) is one of the most widely available laboratory tests globally. Standard CBC parameters such as hemoglobin (Hb), lymphocyte count, and platelet (PLT) count reflect aspects of anemia, immune status, and coagulation function, all of which are relevant to sepsis pathophysiology. Alterations in these parameters have been associated with sepsis severity and poor outcomes in children [6, 7]. Immature granulocytes (IG), measured by automated hematology analyzers, represent early granulopoietic activation during infection and have shown promise as early markers of bacterial infection and sepsis severity [8]. In pediatric populations, IG% has demonstrated better predictive performance for serious bacterial infections than traditional inflammatory markers such as white blood cell count (WBC), absolute neutrophil count (ANC), and CRP [9].

Given the potential prognostic value of CBC parameters and the underexplored role of IG in pediatric sepsis, we aimed to evaluate whether a panel of CBC indices consisting of Hb, lymphocyte count, and platelet count, used jointly in a multivariate logistic regression model, with or without IG, could predict septic shock and in-hospital mortality in children with sepsis in an LMIC setting. This study is the first to investigate the addition of IG to CBC parameters for prognostic modeling in pediatric sepsis within LMICs, where resource constraints necessitate simple, affordable tools. Our analysis incorporated propensity score weighting to minimize baseline imbalances and used net reclassification improvement (NRI) and integrated discrimination improvement (IDI) to assess the incremental value of IG.

Materials and methods

Study design and setting

This was a prospective observational study conducted at a Tertiary Pediatric Centre in Central Vietnam, from July 2023 to July 2025. The study aimed to evaluate the predictive value of CBC indices, with and without IG percentage, for septic shock and mortality in children with sepsis.

Participants and eligibility criteria

Children aged 1 month to 16 years admitted to the pediatric intensive care unit (PICU) or emergency department with suspected sepsis were screened for eligibility. Sepsis was defined according to the International Pediatric Sepsis Consensus Conference criteria, including systemic inflammatory response syndrome with suspected or proven infection [10]. Of 334 initially screened patients, those with missing CBC data, immunodeficiency, hematologic malignancy, chronic steroid use, recent chemotherapy, or incomplete outcome data were excluded. The final cohort included 276 patients, divided into the IG group (n = 52, with IG measurement) and the Non-IG group (n = 224, without IG measurement). IG measurements were clinician-ordered, typically for suspected severe infections. This selective ordering introduces potential indication bias, as patients in the IG group were likely more severely ill. This bias was addressed using propensity score weighting, as detailed below.

Data collection and variables

Demographic and clinical data were collected prospectively from electronic medical records and bedside assessments. Variables included age, sex, vital signs (temperature, heart rate, respiratory rate), Glasgow Coma Scale (GCS), infection origin, underlying diseases, blood culture results, and initial CBC parameters within 24 h of sepsis diagnosis. CBC indices included WBC, neutrophil count, lymphocyte count, Hb, PLT, and IG percentage (where available). Additional laboratory parameters included creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and CRP. Outcomes were septic shock (defined as sepsis with cardiovascular dysfunction requiring vasopressors despite fluid resuscitation) and in-hospital mortality [10]. Data were entered into a secure database with quality checks. IG was measured using Sysmex XN-2000 hematology analyzers within 24 h. At our institution, IG is not part of routine CBC protocols and remains a research parameter, requiring specific analyzer activation; it is selectively requested by physicians for patients at higher perceived risk of bacterial sepsis or rapid progression.

Statistical analysis

Analyses were conducted using R software (version 4.4.2) with packages for data management, modeling, and visualization. The significance level was set at $p < 0.05$. To address potential selection bias (indication bias from clinician-ordered IG in more severe cases), we used descriptive comparisons, predictive modeling, and bias correction methods.

Descriptive and baseline analysis

Patient characteristics were summarized using means with standard deviations for continuous variables and frequencies with percentages for categorical variables. Differences between IG and Non-IG groups were assessed using standardized mean differences (SMDs), with SMD > 0.1 indicating meaningful imbalance. Univariate logistic regression evaluated CBC parameters (WBC, neutrophil, lymphocyte, Hb, PLT, IG) for associations with septic shock and mortality, reporting odds ratios (OR) with 95% confidence intervals (CI). Analyses for WBC, neutrophil, lymphocyte, Hb, and PLT were conducted in the full cohort ($n = 276$) using complete case analysis (no missing data). For IG, univariate analysis was restricted to the subgroup with available IG measurements ($n = 52$).

Propensity score weighting for bias correction

Propensity score (PS) methods addressed imbalances between IG and Non-IG groups. PS was estimated via logistic regression, including baseline covariates (age, sex, temperature, heart rate, infection origin, underlying disease, WBC, neutrophil, lymphocyte, Hb, PLT, mechanical ventilation). Vasopressor use was excluded from the PS model due to its direct relation to septic shock, and AST, ALT, creatinine, and CRP were excluded due to incomplete data. Stabilized and trimmed (1st and 99th percentiles) inverse probability weights (IPW) were applied. Balance was assessed using SMDs, with most covariates achieving SMD < 0.1 after weighting.

Predictive modeling

For the primary analysis, two sets of multivariate logistic regression models were developed:

1. a 'CBC-only' model using Hb, lymphocyte, and PLT, applied to the full cohort ($n = 276$);
2. in the subgroup with available data ($n = 52$), a 'CBC + IG' model adding the percentage of IG.

The performance of these models was compared to assess the incremental value of IG. Both models were re-evaluated using IPW in the IG subgroup to correct for selection bias. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC) with 95% CIs. The incremental value of IG was evaluated using category-free NRI and IDI. Category-free NRI assesses the proportion of patients with improved risk prediction (higher predicted probabilities for events, lower for non-events) without predefined risk thresholds, with 95% CIs derived from 1,000 bootstrap resamples. Decision curve analysis (DCA) was used to evaluate the clinical utility of models across a range of risk thresholds, comparing the net benefit of CBC and CBC + IG models against treating all or none. A bar chart (Fig. 4) displays category-free NRI percentages for events and non-events.

Ethical approval and informed consent

All procedures followed the ethical standards of the institutional review board and the Helsinki Declaration. The study was approved by the Ethics Committee of Hue University of Medicine and Pharmacy under approval number H2023/498. Written informed consent was obtained from the parents or guardians of all participants. An opt-out consent option was provided, allowing parents or guardians to withdraw their child's participation at any point during the study.

Results

Baseline characteristics

Of 334 screened patients, 276 were enrolled (224 Non-IG, 52 IG). Table 1 summarizes baseline characteristics. The IG subgroup had a younger age (1.2 vs. 3.0 years, $p = 0.007$, SMD = 0.18), lower Glasgow Coma Score (11.8 ± 3.5 vs. 13.5 ± 2.6, $p = 0.002$, SMD = 0.54), higher underlying disease prevalence (28.8% vs. 14.7%, $p = 0.016$, SMD = 0.34), lower platelet count (234.1 ± 163.9 vs. 285.1 ± 153.5, $p = 0.034$, SMD = 0.32), and greater mechanical ventilation use (40.4% vs. 21.9%, $p = 0.006$, SMD = 0.40). Mortality was higher in the IG subgroup (51.9% vs. 21.4%, $p < 0.001$), likely driven in part by the higher mechanical ventilation use (40.4% vs. 21.9%, $p = 0.006$), a marker of severe respiratory failure and independent mortality risk in pediatric sepsis, but septic shock incidence was similar (38.5% vs. 27.2%, $p = 0.109$). Other variables (sex, vital signs, laboratory parameters) showed no significant differences ($p > 0.05$, SMD < 0.3). Figure 1 illustrates SMDs, highlighting imbalances in age, Glasgow Coma Score, underlying disease, platelet count, mechanical ventilation, and mortality. These differences confirm the expected indication bias, whereby IG testing was preferentially ordered in more severely ill patients, justifying the use of PS weighting in subsequent analyses.

Univariate associations with outcomes

Table 2 presents univariate logistic regression results. For septic shock, significant predictors were WBC (OR = 0.965, 95% CI: 0.936–0.995, $p = 0.024$), lymphocyte count (OR = 0.819, 95% CI: 0.726–0.922, $p = 0.001$), Hb (OR = 0.787, 95% CI: 0.685–0.905, $p = 0.001$), and PLT (OR = 0.995, 95% CI: 0.993–0.997, $p < 0.001$). For mortality, significant predictors included WBC (OR = 0.960, 95% CI: 0.930–0.992, $p = 0.014$), lymphocyte count (OR = 0.864, 95% CI: 0.771–0.968, $p = 0.011$), Hb (OR = 0.691, 95% CI: 0.593–0.806, $p < 0.001$), PLT (OR = 0.994, 95% CI: 0.992–0.997, $p < 0.001$), and SII (OR = 0.979, 95% CI: 0.961–0.998, $p = 0.033$). Lymphocyte

Table 1 Baseline characteristics of pediatric sepsis patients by IG availability

Variable	Non-IG Subgroup ($n=224$)	IG Subgroup ($n=52$)	*p*-value	SMD
Age, years	3.0 (1.0–6.0)	1.2 (0.6–6.3)	0.007	0.18
Gender (Male, %)	57.6	48.1	0.213	0.19
Temperature (°C)	39.0 ± 0.9	38.9 ± 0.7	0.267	0.18
Heart Rate (bpm)	139.1 ± 26.6	139.8 ± 28.6	0.876	−0.02
Respiration Rate (bpm)	39.4 ± 14.1	36.3 ± 12.2	0.148	0.23
Glasgow Coma Score	13.5 ± 2.6	11.8 ± 3.5	0.002	0.54
Origin of Sepsis (%)				
Respiration	27.2	36.5		
Digestive system	24.1	26.9		
Skin	12.9	0.0	0.037	−0.006
Other	7.2	7.8		
Unknown Origin	28.6	28.8		
Underlying Disease (%)	14.7	28.8	0.016	0.34
White Blood Cell	16.2 ± 9.5	15.3 ± 8.0	0.551	0.10
Neutrophil	11.3 ± 7.8	9.8 ± 6.5	0.191	0.21
Lymphocyte	3.4 ± 3.1	3.6 ± 2.5	0.573	−0.09
Hemoglobin (g/dl)	10.7 ± 1.9	10.2 ± 2.3	0.071	0.26
Platelet	285.1 ± 153.5	234.1 ± 163.9	0.034	0.32
AST	42.1 (27.9–112.2)	54.3 (29.4–171.5)	0.670	0.07
ALT	24.7 (14.0–68.5)	22.5 (11.3–82.8)	0.310	0.18
Creatinine	36.2 (22.8–56.7)	28.0 (19.4–48.1)	0.092	0.07
CRP	119.6 ± 81.0	117.1 ± 81.9	0.867	0.03
Blood Culture Positive (%)	9.4	9.6	0.992	0.002
Mechanical Ventilation (%)	21.9	40.4	0.006	0.40
Vasopressor Use (%)				
1 vasopressor	8.5	13.5	0.260	0.23
Over 1 vasopressor	18.8	25.0		
Septic Shock (%)	27.2	38.5	0.109	-
Mortality (%)	21.4	51.9	< 0.001	-

IG Immature granulocyte, *SMD* Standardized mean difference, *AST* Aspartate aminotransferase, *ALT* Alanine aminotransferase, *CRP* C-reactive protein

count, Hb, and PLT were selected for the CBC predictive model due to their consistent significance for both outcomes in univariate analyses. WBC was not included in the multivariate model because it lacked significance in multiple regression analyses, indicating limited independent predictive value when adjusted for other CBC parameters.

Predictive model performance

Table 3 summarizes logistic regression model performance. In the full cohort ($n=276$), the CBC model (Hb, lymphocyte, PLT) achieved AUCs of 0.725 (95% CI: 0.656–0.795) for septic shock and 0.746 (95% CI: 0.671–0.821) for mortality. In the IG subgroup ($n=52$), the CBC model had AUCs of 0.852 (95% CI: 0.750–0.953) for septic shock and 0.776 (95% CI: 0.646–0.907) for mortality. Adding IG improved AUCs to 0.920 (95% CI: 0.847–0.994) for septic shock and 0.815 (95% CI: 0.694–0.936) for mortality. With IPW, the CBC model in the IG subgroup had AUCs of 0.848 (95% CI: 0.742–0.955) for septic shock and 0.784 (95% CI: 0.654–0.914) for mortality, while the CBC + IG model achieved 0.908 (95% CI: 0.829–0.987) for septic shock and 0.807 (95% CI: 0.683–0.932) for mortality. These IPW-weighted AUCs represent bias-corrected estimates of model performance in the presence of selective IG testing. ROC curves for weighted models are shown in Fig. 2. Decision curve analysis (Fig. 3) demonstrates a slight improvement in net benefit for both septic shock and mortality when adding IG to the CBC model across a range of risk thresholds, indicating modestly enhanced clinical utility.

Incremental value of immature granulocytes

Table 4 presents the incremental value of adding IG in the weighted IG subgroup using category-free NRI. For septic shock, adding IG resulted in a ΔAUC of 0.059 ($p=0.140$), category-free NRI of 0.600 (95% CI: 0.030–1.128), and IDI of 0.108 (95% CI: 0.013–0.228). For mortality, adding IG yielded a ΔAUC of 0.024 ($p=0.503$), category-free NRI of 0.339 (95% CI: −0.151–0.826), and IDI of 0.059 (95% CI: −0.003–0.134). Figure 4 shows category-free NRI percentages, indicating that for septic shock, −8.7% of events and 68.1% of non-events were correctly reclassified, while for mortality, −34.2% of events and 67.3% of non-events were correctly reclassified. This mixed NRI signal indicates that adding IG increases specificity (better identification of patients who will not develop septic shock or die) but reduces sensitivity (worse identification of those who will experience the outcome). The negative NRI for events suggests that adding IG reduced correct classification for events, particularly for mortality, while the positive NRI for non-events indicates improved specificity. The DCA (Fig. 3) shows a slight improvement in net benefit for both outcomes, but the modest NRI and IDI values, combined with non-significant p-values and wide CIs, suggest limited clinical impact of adding IG, especially for septic shock.

Discussion

In pediatric sepsis within a resource-limited setting, a simple prognostic model using only hemoglobin, lymphocyte count, and platelet count from a routine CBC

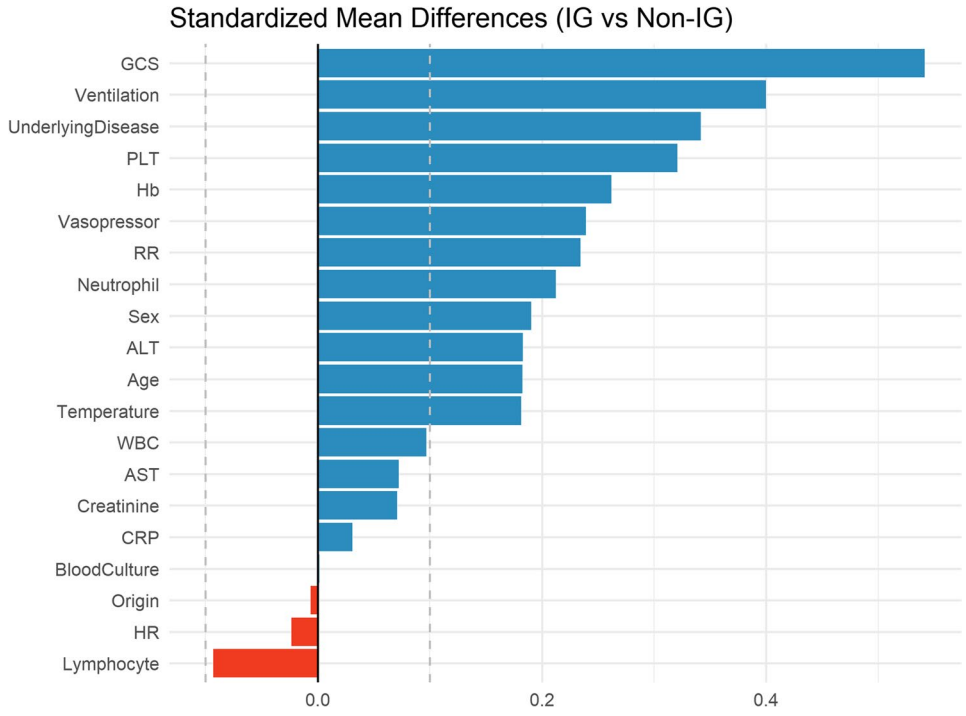

Fig. 1 Standardized Mean Differences (SMDs) between IG and Non-IG groups. Bars represent SMDs for baseline characteristics between IG ($n = 52$) and Non-IG ($n = 224$) groups. Positive SMDs (blue) indicate higher values in the Non-IG group; negative SMDs (red) indicate higher values in the IG group. Dashed lines at ±0.1 denote thresholds for meaningful imbalance; solid line at 0 indicates no difference

Table 2 Univariate logistic regression analysis of CBC parameters for predicting septic shock and mortality

CBC Parameter	Septic Shock OR (95% CI)	*p*-value	Mortality OR (95% CI)	*p*-value
White Blood Cell	0.965 (0.936–0.995)	0.024	0.960 (0.930–0.992)	0.014
Neutrophil	0.979 (0.944–1.014)	0.235	0.969 (0.933–1.006)	0.101
Lymphocyte	0.819 (0.726–0.922)	0.001	0.864 (0.771–0.968)	0.011
Hemoglobin	0.787 (0.685–0.905)	0.001	0.691 (0.593–0.806)	< 0.001
Platelet	0.995 (0.993–0.997)	< 0.001	0.994 (0.992–0.997)	< 0.001
NLR	1.007 (0.994–1.020)	0.296	1.003 (0.99–1.015)	0.661
PLR (x100)	1.022 (0.987–1.059)	0.215	1.02 (0.987–1.053)	0.235
SII (x100)	0.991 (0.976–1.006)	0.240	0.979 (0.961–0.998)	0.033

OR Odds ratio, *CI* Confidence interval, *NLR* neutrophil-to-lymphocyte ratio, *PLR* platelet-to-lymphocyte ratio, *SII* systemic immune-inflammation index

provides moderate-to-good predictive accuracy for septic shock (AUC 0.725) and in-hospital mortality (AUC 0.746). Adding IG offers minimal incremental benefit, confirming that standard CBC parameters remain the most practical and feasible tool for risk stratification in LMICs.

Baseline characteristics such as age, presence of underlying diseases, and signs of organ dysfunction significantly influence disease progression and outcomes. Younger children are particularly susceptible due to underdeveloped immune responses and limited physiological reserves, often leading to rapid deterioration. In our study, the IG subgroup exhibited distinct baseline features, including younger age (median 1.2 years vs. 3.0 years in the Non-IG group), a higher prevalence of underlying diseases (28.8% vs. 14.7%), and increased respiratory failure as indicated by greater mechanical ventilation requirements (40.4% vs. 21.9%). These factors likely contributed to the elevated mortality rate observed in the IG group (51.9% vs. 21.4%), reflecting a selection bias where IG testing was preferentially ordered for more critically ill patients with complex comorbidities and respiratory compromise. This underscores the importance of accounting for such imbalances in analyses, as addressed through propensity score weighting in our study. The absence of differences in initial vital signs and laboratory indices does not contradict known mortality predictors; rather, it reflects the early, compensatory phase of sepsis in children, where standard markers (e.g., WBC, CRP, tachycardia) are elevated across all severity groups at presentation and gain prognostic value only with serial assessment or in combination with clinical risk factors (e.g., age, comorbidities, need for ventilation) [1, 3]. Clinician ordering of IG was thus guided by holistic risk

Table 3 Performance of multivariate logistic regression models for predicting septic shock and mortality

Outcome	Model	Cohort	Predictors	AUC	95% CI
Septic Shock	CBC Model	Full cohort (*n* = 276)	Hb + Lymphocyte + Platelet	0.725	0.656–0.795
Septic Shock	CBC Model	IG subgroup (*n* = 52)	Hb + Lymphocyte + Platelet	0.852	0.750–0.953
Septic Shock	CBC Model	IG subgroup (*n* = 52)	Hb + Lymphocyte + Platelet + IG	0.920	0.847–0.994
Septic Shock	CBC Model	IG subgroup (IPW)	Hb + Lymphocyte + Platelet	0.848	0.742–0.955
Septic Shock	CBC + IG Model	IG subgroup (IPW)	Hb + Lymphocyte + Platelet + IG	0.908	0.829–0.987
Mortality	CBC Model	Full cohort (*n* = 276)	Hb + Lymphocyte + Platelet	0.746	0.671–0.821
Mortality	CBC Model	IG subgroup (*n* = 52)	Hb + Lymphocyte + Platelet	0.776	0.646–0.907
Mortality	CBC Model	IG subgroup (*n* = 52)	Hb + Lymphocyte + Platelet + IG	0.815	0.694–0.936
Mortality	CBC Model	IG subgroup (IPW)	Hb + Lymphocyte + Platelet	0.784	0.654–0.914
Mortality	CBC + IG Model	IG subgroup (IPW)	Hb + Lymphocyte + Platelet + IG	0.807	0.683–0.932

AUC Area under the receiver operating characteristic curve, *CI* Confidence interval, *IPW* Inverse probability weighting, *CBC* Complete blood count, *Hb* Hemoglobin, *IG* Immature granulocyte, *NRI* Net reclassification improvement, *IDI* Integrated discrimination improvement, *DCA* Decision curve analysis

assessment rather than isolated lab or vital sign thresholds, explaining the observed selection pattern.

This prospective study evaluated the predictive value of CBC indices, with and without IG, for septic shock and mortality in pediatric sepsis at a tertiary care hospital in Vietnam. Our findings demonstrate that a CBC-based model including Hb, lymphocyte, and PLT has moderate to good discriminative ability for predicting septic shock (AUC 0.725 in the full cohort, 0.848 in the weighted IG subgroup) and mortality (AUC 0.746 in the full cohort, 0.784 in the weighted IG subgroup). Notably, this simple model using only Hb, lymphocyte, and PLT achieved robust predictive performance in the full cohort (AUCs 0.725 and 0.746), underscoring the clinical utility of universally available CBC parameters as practical prognostic tools in resource-limited LMIC settings. The addition of IG to the CBC model improved AUCs in the IG subgroup (0.908 for septic shock, 0.807 for mortality with IPW), but the incremental value, as assessed by category-free NRI and IDI, was modest and not statistically significant, particularly for septic shock (NRI = 0.600, $p = 0.140$; IDI = 0.108). For mortality, the NRI was also modest (NRI = 0.339, $p = 0.503$; IDI = 0.059), with a notable reduction in correct classification for events (−34.2%) but improved classification for non-events (67.3%). DCA indicated a slight improvement in net benefit for both outcomes when adding IG, suggesting limited clinical utility, especially in resource-constrained settings.

Our CBC panel model compares favorably with established and emerging pediatric sepsis prognostic tools, particularly in LMIC contexts where resource constraints limit advanced diagnostics. For instance, the Pediatric Sepsis Biomarker Risk Model (PERSEVERE-II), which integrates five plasma biomarkers with clinical phenotypes, yields AUCs of 0.80–0.88 for mortality in septic shock cohorts [7, 11]. Similarly, the pSOFA and PELOD-2 scores—validated in LMIC meta-analyses-demonstrate pooled AUCs of 0.86 and 0.83 for mortality, respectively, but require organ dysfunction assessments

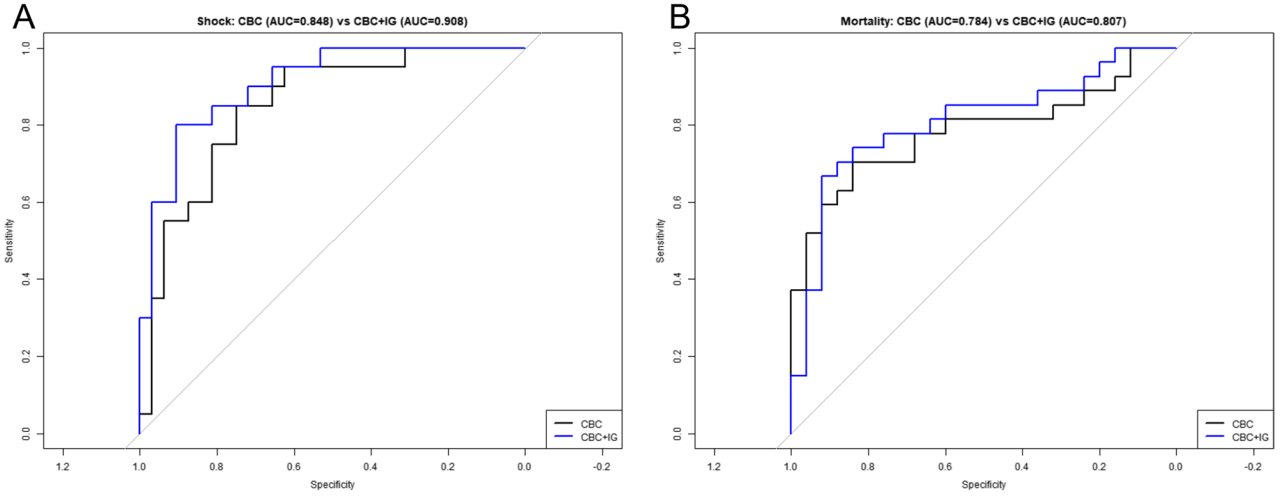

Fig. 2 Receiver Operating Characteristic (ROC) Curves for Weighted Models in the IG Subgroup. **A** ROC curves for predicting septic shock using CBC (black) and CBC + IG (blue). **B** ROC curves for predicting mortality using CBC (black) and CBC + IG (blue). Models weighted using inverse probability weights in the IG subgroup (*n* = 52)

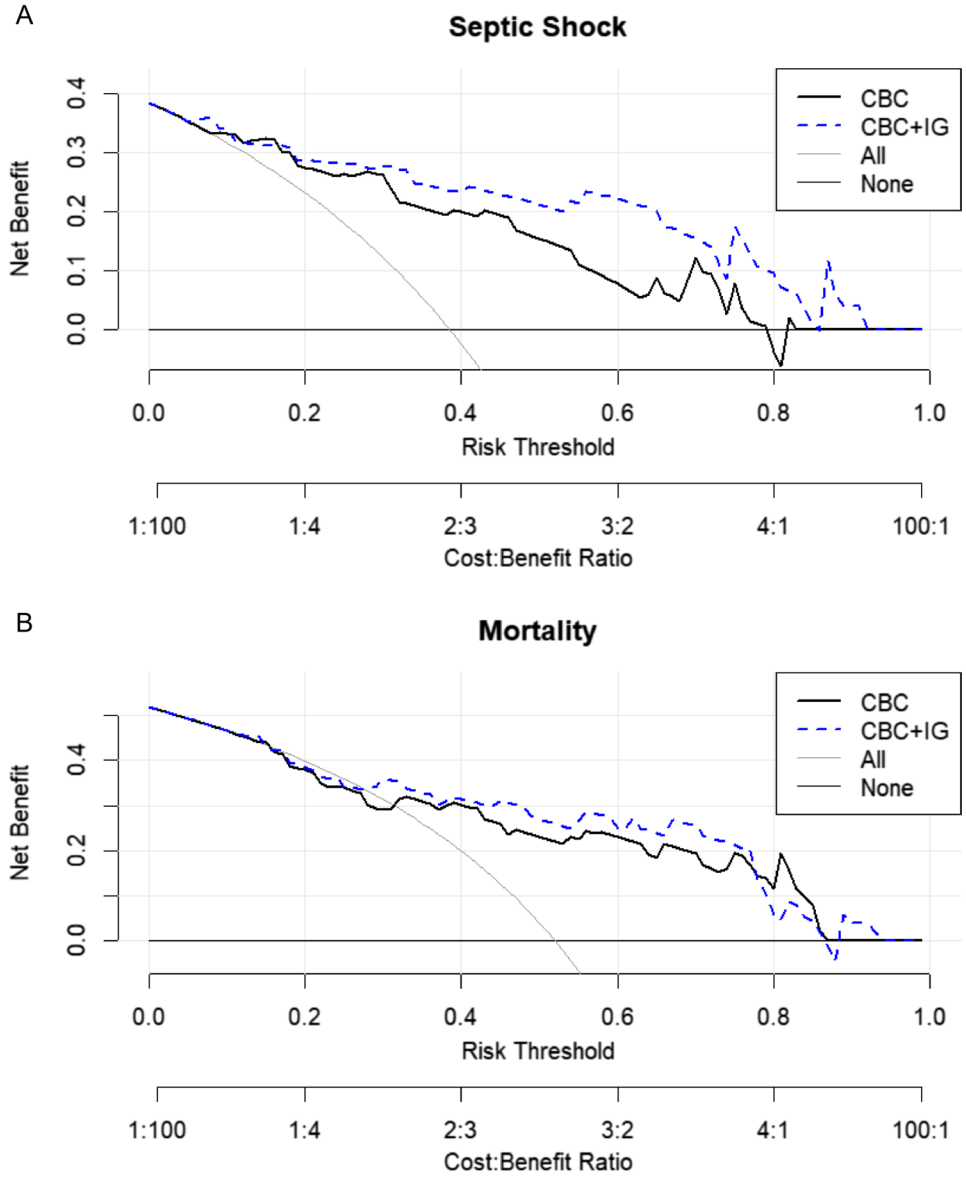

Fig. 3 Decision Curve Analysis (DCA) for Weighted Models in the IG Subgroup.**A** Septic Shock: Net benefit of the weighted CBC model (black) and CBC + IG model (blue) compared to treating all (gray dashed) or none (horizontal line at 0) across risk thresholds. **B** Mortality: Net benefit of the weighted CBC model (black) and CBC + IG model (blue) compared to treating all (gray dashed) or none (horizontal line at 0). Higher net benefit indicates better clinical utility at a given risk threshold. CBC includes Hemoglobin, Lymphocyte, and Platelet counts; IG denotes Immature Granulocytes. Data were derived from the IG subgroup with inverse probability weighting to adjust for baseline imbalances

that may not be feasible at initial presentation [4]. Recent machine learning (ML) models leveraging electronic health records and Phoenix Sepsis Score criteria achieve AUROCs of 0.85–0.96 for early detection in emergency or PICU settings [1, 5].

The CBC parameters (Hb, lymphocyte count, PLT) were selected for the predictive model based on their consistent significance in univariate analyses for both septic shock and mortality, aligning with prior studies that highlight their relevance to prior sepsis pathophysiology. Low Hb reflects anemia, which may exacerbate tissue hypoxia in sepsis, while lymphopenia indicates immune suppression, and thrombocytopenia is linked to coagulation dysfunction [12, 13]. Notably, WBC was not included in the multivariate model due to its lack of significance in multiple regression analyses, suggesting that its predictive value is diminished when adjusted for other CBC parameters. This finding is consistent with studies indicating that WBC alone is a less specific marker for sepsis severity compared to lymphocyte or platelet counts [14, 15].

Traditional inflammatory indices derived from CBC, such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic

Table 4 Incremental predictive value of adding IG to CBC model in weighted IG subgroup

Index		Outcome	
		Septic Shock	Mortality
Δ AUC	Value	0.059	0.024
	95% CI	−0.009–0.155	−0.04–0.1
	p-value	0.140	0.503
NRI	Value	0.600	0.339
	95% CI	0.030–1.128	−0.151–0.826
IDI	Value	0.108	0.059
	95% CI	0.013–0.228	−0.003–0.134

Δ AUC Change in area under the curve, *NRI* Net reclassification improvement (category-free), *IDI* Integrated discrimination improvement, *IG* Immature granulocyte, *CBC* Complete blood count

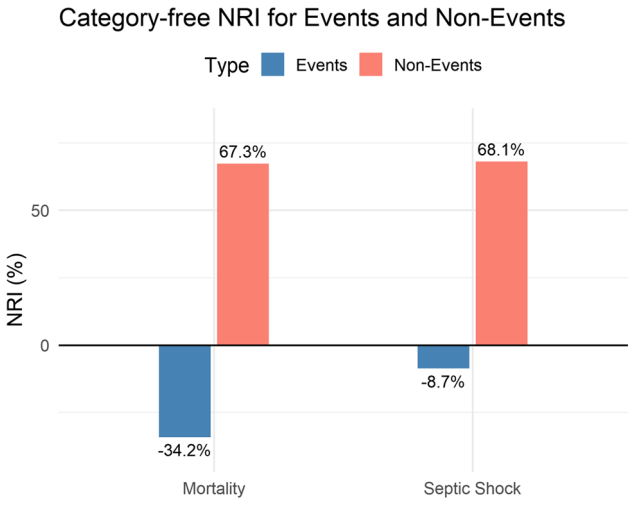

Fig. 4 Net Reclassification Improvement (NRI) for adding IG to CBC model. Bar chart showing the percentage of events and non-events reclassified after adding IG to the CBC model for septic shock and mortality in the IG subgroup (n = 52). Models were weighted using inverse probability weights

immune-inflammation index (SII), have been extensively investigated as prognostic markers in sepsis, particularly in adults, where elevated NLR and PLR are associated with increased mortality and disease severity [16–18]. In pediatric populations, these indices have shown promise in some studies; for example, a rise in NLR and PLR has been linked to higher mortality in pediatric sepsis, and PLR has been identified as a risk factor for sepsis mortality in children [7, 19]. Similarly, SII, which incorporates neutrophil, platelet, and lymphocyte counts, has been associated with pediatric sepsis outcomes in critical care settings [20]. NLR and PLR have also demonstrated diagnostic utility in neonatal sepsis, with comparable performance for identifying severe cases [21]. However, results in children are inconsistent, potentially due to physiological variations [11, 22].

In our study, we evaluated NLR, PLR, and SII using the available data. NLR and PLR were not significantly associated with either septic shock or mortality (p >0.05), while SII showed a slight association with mortality (OR = 0.979, 95% CI: 0.961–0.998, p = 0.033) but not with septic shock. These indices were not selected for the final model due to their limited independent predictive value. This lack of significance may be attributed to specific physiological features in children, where neutrophil and lymphocyte counts vary markedly with age. For instance, neonates exhibit relative lymphocytosis, with NLR increasing progressively from infancy to adolescence due to rising neutrophil counts and declining lymphocyte proportions. Such age-related changes can lead to wide variability in NLR, PLR, and SII across pediatric age groups, potentially reducing their prognostic reliability in heterogeneous cohorts like ours (age 1 month to 16 years) [11, 22]. In contrast, absolute values of Hb, lymphocyte, and PLT may be more directly reflective of sepsis-induced alterations (e.g., anemia, lymphopenia, thrombocytopenia) and less influenced by developmental physiology, enabling the construction of a novel predictive model tailored to pediatric sepsis. This model represents a simple, cost-effective alternative to ratio-based indices, particularly in LMICs where advanced diagnostics are limited [3, 4].

The modest improvement observed with IG addition aligns with prior research suggesting that IG percentage is a promising early marker of bacterial infection and sepsis severity [8, 9]. For instance, Güngör et al. (2021) found that IG percentage outperformed traditional markers like WBC and CRP in predicting serious bacterial infections in children [9]. However, our study found that IG's incremental value was limited, particularly for septic shock, where the category-free NRI showed a negative reclassification for events (−8.7%) but a positive reclassification for non-events (68.1%). For mortality, the NRI was also modest (−34.2% for events, 67.3% for non-events), indicating improved specificity but reduced sensitivity when IG was added. This pattern arises because IG reflects early granulopoietic activation, which is prognostically informative in patients with adequate physiological reserve (correctly reclassified as non-events) but becomes non-discriminatory in advanced, irreversible organ dysfunction (events). In a high-mortality cohort like ours (>20%), the narrow therapeutic window limits IG's ability to predict imminent shock or death, despite its biological relevance. Thus, IG enhances the model's ability to "rule out" progression but adds little to "rule in" risk among the sickest children. The non-significant p-values and wide confidence intervals for NRI and IDI further confirm the limited clinical impact of adding IG, consistent with the modest AUC gains.

The DCA results, showing a slight increase in net benefit for both outcomes, suggest that adding IG may offer marginal clinical utility in specific contexts, such as settings with access to automated hematology analyzers

capable of measuring IG. However, the high cost and limited availability of such analyzers in low- and middle-income countries (LMICs), where pediatric sepsis burden is greatest [3, 4], reduce the practicality of routine IG measurement. This is particularly relevant given the modest incremental benefit observed, which may not justify the additional resource burden in resource-constrained settings [4].

This study's strengths include its prospective design, robust statistical methods, and focus on CBC, a widely accessible test suitable for LMICs [1, 2]. Limitations include the small IG subgroup (n = 52), potential selection bias from testing only suspected severe cases, incomplete laboratory data for some confounders, and the single-center design in Vietnam, which may limit generalizability [5]. Future research should validate these findings in larger, multicenter LMIC cohorts to clarify the incremental value of IG and confirm the utility of the CBC model (Hb, lymphocyte, PLT) [6]. Combining CBC indices with clinical scores or exploring other low-cost biomarkers may further improve prediction, while cost-effectiveness and age-stratified analyses could guide implementation in resource-limited settings.

Conclusion

This study, the first in an LMIC setting, shows that standard CBC parameters provide moderate-to-good accuracy for predicting septic shock and mortality in pediatric sepsis, outperforming common indices and remaining feasible in resource-limited environments. Adding IG modestly improved AUCs but offered limited clinical value due to cost and availability. Thus, standard CBC remains a practical, cost-effective tool for risk stratification, with further validation needed to strengthen pediatric sepsis care in LMICs.

Abbreviations

AUC	Area under the receiver operating characteristic curve
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
AST	Aspartate aminotransferase
CBC	Complete blood count
CI	Confidence interval
CRP	C-reactive protein
DCA	Decision curve analysis
GCS	Glasgow Coma Scale
Hb	Hemoglobin
IDI	Integrated discrimination improvement
IG	Immature granulocyte
IPW	Inverse probability weighting
LMIC	Low- and middle-income country
NLR	Neutrophil-to-lymphocyte ratio
Non-IG	Non–immature granulocyte subgroup
NRI	Net reclassification improvement
OR	Odds ratio
PICU	Pediatric intensive care unit
PLR	Platelet-to-lymphocyte ratio
PLT	Platelet count
PS	Propensity score
ROC	Receiver operating characteristic
SII	Systemic immune-inflammation index
SMD	Standardized mean difference
WBC	White blood cell count

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Code availability

The code used for data analysis and figure generation in this study is publicly available at GitHub: https://github.com/AllabHuemed/pediatric-sepsis-analysis.

Authors' contributions

Chau-Duc Nguyen-Huu conceived and supervised the study. Quoc Bao Vo, Hoang Le, Tuan Tai Manh, and Thi Lan Nguyen collected clinical data. Van-Tuy Nguyen performed data analysis and drafted the initial manuscript. Nhu-Huy Pham, Hoang Duy Phan, Hanh Chan T. Tran, Kieu Loc Pham, Thi Tam Dang, Thi Na Truong, Ha My Ho, and Hoang Bach Nguyen contributed to data interpretation, critical manuscript revision, and provided important intellectual content. All authors read and approved the final manuscript.

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Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to restrictions to protect participant confidentiality and compliance with ethical approvals.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the ethical standards outlined in the 1964 Helsinki Declaration and its subsequent amendments. Ethical approval was obtained from the Ethics Committee of Hue University of Medicine and Pharmacy, Hue City, Vietnam (Approval Number: H2023/498, Approval Date: May 24, 2023).

Consent for publication

Written informed consent was obtained from the parents or legal guardians of all pediatric participants prior to enrollment. Personal information, including names, phone numbers, and addresses, was not collected, and all data were anonymized and maintained with strict confidentiality to protect participant privacy.

Competing interests

The authors declare no competing interests.

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