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Diagnostic Threshold of Immature Granulocytes in Pediatric Infections

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Abstract

Objectives: This study aimed to assess the optimal cutoff and the diagnostic utility of IG in common pediatric infections.
Methodology: This case-control study included children aged 1–17 years presenting with suspected infection or sepsis between December 2024 and July 2025. Clinical and laboratory parameters (WBC, ANC, IG%, and absolute IG count) were recorded within 24 hours of presentation and compared with age-matched non-infected controls. Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate diagnostic performance and calculate the area under the curve (AUC).
Results: A total of 150 patients (85 males, 65 females) with a mean age of 5.74 ± 4.59 years were included. Over 80% had gastrointestinal or respiratory infections. Compared with controls, patients showed significantly higher WBC and ANC ($p < 0.001$), IG% (0.91 ± 1.31 vs 0.22 ± 0.09; $p = 0.001$), and absolute IG count (0.13 ± 0.26 vs 0.02 ± 0.01 $\times 10^9$/L; $p < 0.001$). An IG% cutoff >0.25 yielded 82.0% sensitivity (95% CI 75.1–87.3) and 68.0% specificity (95% CI 60.2–74.9). Multivariable analysis confirmed IG% as an independent predictor of infection ($p < 0.001$).
Conclusion: IG% is a useful early biomarker that can be used in conjunction with traditional leukocyte indices (WBC and ANC) to detect pediatric infections, demonstrating improved overall diagnostic accuracy and facilitating timely clinical decision-making.
Key words: Pediatric sepsis, immature granulocytes, C-reactive protein, procalcitonin, biomarker.

Introduction

Fever is one of the most common reasons why children are admitted to the paediatric emergency department (PED), accounting for a large percentage of hospital admissions. [1] While most febrile illnesses in children are caused by self-limiting viral infections, a small but significant proportion result from severe bacterial infections (SBI).[2] which may progress to life-threatening organ dysfunction leading to systemic inflammatory response syndrome (SIRS), or sepsis, leading to mortality and morbidity.[3] Early detection is often difficult because many children present with mild or nonspecific symptoms in the early stages of illness. Commonly used conventional laboratory markers, including CBC parameters such as white blood cell (WBC) count, absolute neutrophil count (ANC), C-reactive protein (CRP), and procalcitonin (PCT), can help with clinical decision-making, but their diagnostic accuracy varies, and no single marker is completely convincing.[4] Additionally, other biomarkers like interleukin-8 (IL-8), CD64, interleukin-18 (IL-18), and serum lactate have been utilized for sepsis.[5, 6] However, their utility is often restricted due to limited availability, high costs, and modest specificity and sensitivity, underscoring the need for alternative markers that are both reliable and readily accessible, particularly in low-resource settings.[6]

Immature granulocytes (IG) are myeloid precursors (including promyelocytes, myelocytes, and metamyelocytes) that are normally absent in the peripheral blood (<1%) but are released into the bloodstream in response to infection, inflammation, and physiological stress, and are significantly elevated in conditions such as sepsis.[7] Traditionally, IG detection relied on conventional blood smear inspection, which is time-consuming and observer-dependent. Nowadays, modern automated haematology analyzers, such as the Sysmex XE and XN series, utilize fluorescence flow cytometry to automatically measure IG parameters, enabling quick, precise, and cost-effective determination of IG count and percentage directly from peripheral blood samples, eliminating the need for manual microscopy.[8] These IG parameters are identified by a distinct cluster above mature neutrophils in the white blood cell differential (WDF) channel and distinguished by forward-scatter light (FSC), side-scatter light (SSC), and side fluorescent light (SFL). While comprehensive

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clinical evaluation and the integrated use of several markers cannot be replaced by a single biomarker, the automatic availability of IG parameters from routine CBC supports their use as a helpful adjunct in pediatric emergency diagnosis algorithms.[9] IG% and absolute IG count have emerged as promising markers for predicting infection and sepsis[9], but they have not yet been routinely incorporated into diagnostic tools for infections.[10] Few studies have reported varying cut-offs, with an absolute IG count >0.3 × 10⁹/L or an IG% >3% demonstrating high specificity for bacterial infection or sepsis.[11-13] In contrast, lower limits have also been observed, depending on the patient population and clinical context; such as IG of 2% was able to exclude sepsis in adults.[12] More research has been conducted in adult populations, where IG elevation has been linked to a variety of acute diseases, including severe infections, appendicitis, pancreatitis, septic complications in burns, and ICU patients, with some studies indicating that it may outperform traditional markers like CRP in predicting sepsis.[13-19] In children, IG has been evaluated in the context of COVID-19, multisystem inflammatory syndrome (MIS-C), appendicitis, urinary tract infection, critical care, and neonatal sepsis, but its utility for early sepsis detection and for detecting bacterial infection after the neonatal period is unknown.[19-26] Since IG measurement is quick, affordable, convenient, and an integrated part of routine complete blood count analysis, its usefulness has been evaluated in resource-limited settings and developing countries. The immature-to-total granulocyte (I/T) ratio and related hematological parameters have demonstrated promise as effective markers in guiding judicious antibiotic usage and detecting early-onset sepsis.[26-30]

The purpose of this study is to assess the diagnostic accuracy of IG% and compare it with standard infection markers (WBC, ANC, and CRP) for predicting infections in pediatric patients (ages 1-17 years) presenting to the pediatric emergency or outpatient department with fever or suspected infection.

Methodology

This was a case-control study carried out at Aga Khan University Hospital (AKUH) in Karachi, Pakistan, from December 2024 to July 2025. The study was approved by the institutional ethical review committee [ERC# 2025-9338-35931], and the data were anonymized for subsequent statistical analysis.

The cases included hospitalized patients aged 1 to 17 years of any gender who presented to the PED with a clinical diagnosis of infections and sepsis. Patients younger than 1 year or older than 17 years, outpatients, those with underlying hematologic malignancies, and individuals receiving chemotherapeutic drugs, myelosuppressive drugs, immunosuppressants, steroids, G-CSF, or antibiotics on the first day of admission were excluded. Patients with missing clinical or laboratory data were also excluded. Controls were children attending outpatient clinics for routine follow-up or nonspecific complaints, who were clinically stable and had normal CBC results.

Patients presenting with fever, hyperthermia, tachypnoea, and tachycardia underwent extensive clinical and laboratory evaluations to diagnose bacterial, fungal, viral, or protozoal infections. They were further classified by systemic involvement (gastrointestinal, respiratory, CNS, and genitourinary infections) and sepsis. The definitions from the 'International Pediatric Sepsis Consensus Conference' were used to diagnose sepsis. The Pediatric Sequential Organ Failure Assessment (SOFA) score (formerly known as Sepsis-Related Organ Failure Assessment), which is considered significantly associated with sepsis (Third International Consensus Definitions for Sepsis and Septic Shock [Sepsis-3]), was used to assess organ dysfunction in severely ill patients.

The patient's age, gender, diagnosis, mode of admission, and length of hospital stay were recorded. Clinical parameters, including heart rate, respiratory rate, and body temperature, were recorded. Initial 24-hour laboratory results, including complete blood count (CBC) (with WBC count, ANC, IG%, and IG absolute), procalcitonin, and CRP, were documented for each patient. Relevant cultures from blood, cerebrospinal fluid, respiratory samples (including sputum, ear, nasal, ENT, and pleural fluids), urine, fungal infections, AFB, and other miscellaneous samples (e.g., synovial or other body fluids) were collected when available. CBC was performed using a Sysmex XN-1000 automated hematology analyzer, which classifies WBCs via flow cytometry. A two-dimensional scattergram displaying side fluorescent light (SFL) intensity on the X-axis and

forward-scattered light (FSC) on the Y-axis is generated to clearly identify lymphocytes, monocytes, eosinophils, basophils, neutrophils, and debris. Based on size, granularity, and nucleic acid content of WBCs, the Sysmex XN series evaluates the IG count in the white cell differential channel. Promyelocytes, myelocytes, and metamyelocytes comprise the IG fraction (excluding blasts and band cells), and this IG cluster appears directly above the neutrophil cluster in the bi-parametric histogram of side scatter and fluorescence.[26]

Data were analyzed using SPSS version 26.0 (IBM Corp). Continuous and categorical variables were expressed as mean ± standard deviation (SD) and frequencies (n) or percentages (%), respectively. CBC parameters were compared between cases and controls using independent t-tests, and p-values <0.05 were considered statistically significant. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of hematological biomarkers for detecting pediatric infections. Optimal cut-offs were determined using the Youden index. Area under the curve (AUC), sensitivities, specificities, positive predictive values (PPV), and negative predictive values (NPV) were calculated for each marker. An AUC of 0.5 was considered a poor discriminator, while an AUC of 1.0 represented a perfect classification model. Multivariate binary logistic regression analysis was conducted to identify independent predictors of infection, reporting odds ratios (ORs) with 95% confidence intervals (CI).

Results

During the study period, 150 pediatric patients (85 males and 65 females) with suspected infection were enrolled; the mean ± SD age was 5.74 ± 4.59 years. Tachycardia (n=140, 93.3%), tachypnoea (n=144, 96.0%), and fever (n=68, 45.3%) were the primary presenting symptoms. Most patients were admitted either to the Ward (n=90, 60%) or to the PICU (n=20, 13.3%), while 40 patients (26.6%) were discharged from the emergency department. Twenty patients (13.3%) were critically ill, including 11 (7.3%) with confirmed sepsis. Most patients had gastrointestinal infections (n=86, 57.3%) and respiratory tract infections (n=40, 26.7%), followed by urinary tract infections, central nervous system infections, and other miscellaneous infections (each n=8, 5.3%). Of the 11 septic patients admitted to the ICU, 3 (27%) had lower respiratory tract infection, 4 (36.3%) had gastrointestinal infection, and the remaining 4 (36%) had bacteraemia, urinary tract infection, central nervous system infection, or post-surgical infection. The mean ± SD SOFA score for the 20 patients in the PICU was 7.9 ± 3.65. Nine of the 150 patients (6%) died due to underlying sepsis and cardiopulmonary arrest.

Laboratory findings are summarized in Table I. This indicates that microbiological testing results varied by specimen type. Blood cultures were performed in 116 patients; 44 (37.9%) were positive. Respiratory tract cultures had a high positivity rate of 14/23 (60.9%). Serological testing detected malaria and dengue in 1 of 4 tested cases (25% each). Inflammatory biomarkers showed high diagnostic value, with elevated serum lactic acid in 18 of 20 patients (90%), raised procalcitonin in 19 of 30 patients (63.3%), and increased C-reactive protein in 66 of 95 patients (69.4%). Of the 59 patients with confirmed pathogen detection, bacterial pathogens predominated; gram-negative rods were the most frequently identified pathogens (n=25, 42.3%), followed by gram-positive cocci (n=16, 27%), mixed (n=9, 15.2%) pathogens, acid-fast bacilli (n=3, 5%), gram negative coccobacillus (n=2, 3.4%) and gram-positive rod (n=1, 1.7%). The least common organisms identified were protozoa (n=2, 3.4%) and viruses (n=1, 1.7%).

Table II presents a comparative analysis of CBC parameters between patients with infection (cases) and those without (controls). It shows lower mean hemoglobin and higher WBC (14.27 ± 22.22 x 10^9/L) and ANC (7.95 ± 6.61 x 10^9/L) in patients than in the control group (Figure 2A, 2B). Mean IG (0.91 ± 1.31% vs. 0.22 ± 0.09%) and absolute IG (0.13 ± 0.26 vs. 0.02 ± 0.01, p < 0.001) were also significantly higher in cases than in the controls (p = 0.001) (Figure 2C, 2D). Median IG % was 1.9 (IQR 0.9-3) in 11 patients with sepsis, significantly higher than in 139 non-sepsis patients (0.40, IQR 0.3-0.7), p=0.003. Similarly, median IG absolute was 0.23 (IQR 0.09-0.85) in patients with sepsis and 0.05 (IQR 0.03-0.08) in patients without sepsis (p<0.001). Moreover, the IG count and the IG% were significantly elevated in deceased patients. Median IG absolute was 0.23 (IQR 0.18–0.39) and IG% 1.70 (IQR 0.90–2.85) in non-survivors, while they were 0.05 (IQR 0.03–0.09) and 0.40 (IQR 0.30–0.75), respectively, in survivors (p = 0.015 and < 0.001).

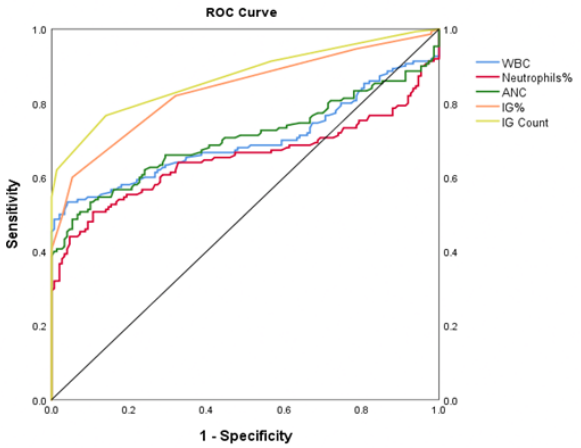

Figure 1. ROC analysis demonstrated that IG absolute count showed the highest diagnostic accuracy (AUC 0.867), followed by IG% (AUC 0.827), while WBC and ANC showed moderate discriminatory power.

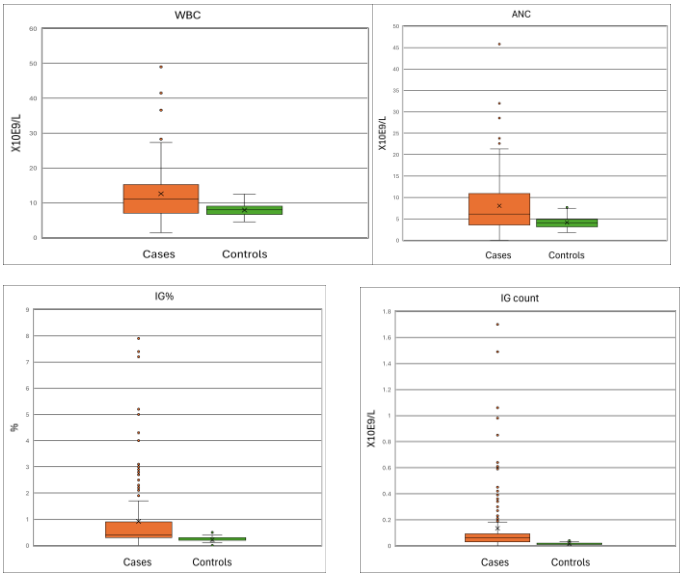

Figure 2. Box-and-whisker plot showing the distribution of white blood cell (WBC) counts, absolute neutrophil count (ANC), immature granulocytes (IG) %, and IG absolute count between cases and controls (represented by A, B, C, and D).

Table I: Demographic, clinical features, and laboratory investigations of cases. (n=150)		
Parameters	Units	Results
Age (in years)	Mean ± SD	5.74 ± 4.59
Sex	(M/F)	85/65
Clinical features		
Febrile	n (%)	68 (45.3)
Tachycardia		140(93.3)
Tachypnoea		144 (96.0)
SOFA score*	(Mean ± SD)	7.9 ± 3.65
Status		
Discharged	n (%)	40(26.6)
Floor Ward		90 (60)
ICU		20 (13.3)
Critical		
Yes	n (%)	20(13.3)
No		125 (83.3)
Organ dysfunction and lab-proven infection		
Yes	n (%)	11 (7.3)
No		139 (92.7)
Outcome		
Discharged	n (%)	127 (71.3)
Fatality		9 (5.1)
Lost to follow-up		12 (6.7)
Not known		2 (1.1)
Cultures		
	Number of tests performed N	Positive/abnormal results n (n/N%)
Blood	116	44 (37.9)
Respiratory tract	23	14 (60.9)
Pleural	1	1 (100.0)
Urine	48	6 (12.5)
Stool	15	2 (13.3)
AFB	4	1 (25.0)
CSF	1	1
Knee aspirate	1	1
Fungal	1	1
Genitourinary	1	1
Serology		
Malaria	4	1 (25.0)
Dengue	4	1 (25.0)
Amoebiasis	1	1
Molecular studies		
Multiplex PCR	2	0 (0.0)
PCR assay for MTB**	12	2 (16.6)
Blood Chemistry		
Serum lactic acid	20	18 (90)
Serum procalcitonin	30	19 (63.3)
C-reactive protein	95	66 (69.4)

Table II: Comparison of complete blood count parameters between 150 cases and 150 controls.				
Variables	Reference intervals	Cases	Controls	*p*-value*
Hemoglobin	10-16.6 g/dl	10.78 ± 2.35	12.65 ± 1.08	< 0.001
Platelets	150-550 x 109/L	312.29 ± 158.52	313.92 ± 76.82	0.91
WBC	4.6-16 x 109/L	14.27 ± 22.22	7.88 ± 1.63	< 0.001
ANC	1.5 – 8 x 109/L	7.95 ± 6.61	4.15 ± 1.25	< 0.001
ALC	6-9 x 109/L	3.70 ± 4.65	2.81 ± 0.85	0.022
AMC	0.2 – 1 x 109/L	1.01 ± 1.06	0.60 ± 0.15	<0.001
IG %	0-1%	0.91 ± 1.31	0.22 ± 0.09	<0.001
IG Count	0.0-0.12 x 109/L	0.13 ± 0.26	0.02 ± 0.01	<0.001

Table III: Diagnostic performance of complete blood count parameters for pediatric infection.							
CBC parameters	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Cut-off Used	AUC	P-value
WBC x 10^9/L	94.0	67.1	52.7	96.7	10.7	0.694	<0.001
ANC x 10^9/L	82.5	65.5	53.3	88.7	5.65	0.692	<0.001
Neutrophils %	60.0	71.3	67.7	64.1	56.40	0.650	<0.001
IG %	82.0	64.0	69.5	78.0	0.25	0.827	<0.001
IG absolute x 10^9/L	84.5	78.6	76.7	86.0	0.02	0.867	<0.001

Table III shows that overall, WBC, ANC, IG%, and IG absolute count have high sensitivities ranging from 82% to 94%, along with good NPVs of 78% to 97% for differentiating pediatric infections from non-infections. IG parameters demonstrated superior diagnostic performance compared with traditional leukocyte measures, with higher specificity (78.6%) and PPV (76.7%). ROC analysis (Figure 1) indicated limited discriminative ability for WBC and ANC, each with an AUC of about 0.60, while IG showed good discrimination with an AUC greater than 0.80. At an IG% cut-off of >0.25, sensitivity and specificity for identifying pediatric infection were 82.0% (95% CI 75.1–87.3) and 68.0% (95% CI 60.2–74.9), respectively. Increasing the cut-off to >0.40 improved specificity to 97.3% (95% CI 93.3–99.0) at the expense of sensitivity (49.3%, 95% CI 41.4–57.3). The AUC for IG% was 0.83, indicating good overall discriminative performance.

Table IV: Multivariable logistic regression for pediatric infection.				
Parameter	β (SE)	Odds Ratio (OR)	95% CI	p-value
IG%	8.17 (1.37)	3525	241 – 51,700+	<0.001
WBC	0.23 (0.08)	1.25	1.07 – 1.47	0.007
ANC	0.07 (0.11)	1.07	0.86 – 1.32	0.54

Multivariable logistic regression (Table IV) revealed that IG% was independently associated with infection in pediatric patients ($p < 0.001$). The large odds ratio reflects the narrow distribution and scaling of IG values. Each 0.1% increase in IG was associated with roughly a twofold increase in the odds of infection. WBC showed a moderate association, while ANC was not independently associated after adjustment.

Discussion

This study emphasizes that immature granulocyte (IG) parameters, particularly the absolute IG count and IG percentage (IG%), serve as effective hematological biomarkers for detecting infection in febrile pediatric patients presenting to the emergency department. IG count showed the highest discriminatory ability among CBC parameters (AUC 0.867; cut-off 0.02 × 10^9/L; sensitivity 84.6%, specificity 78.7%), followed by IG% (AUC 0.827; cut-off 0.25%), demonstrating good sensitivity (82%) however, moderate specificity 64%).

Despite this, IG% outperformed traditional indices like WBC (AUC 0.694) and ANC (AUC 0.692). Non-survivors had higher median IG values (IG count 0.23 × 10^9/L and IG% 1.70%) compared to survivors. Multivariable regression analysis indicated that IG% remains an independent predictor of infection, underscoring its complementary role in early infection diagnosis. Immature granulocytes should therefore be used as an adjunct marker to aid clinical decision-making in combination with other laboratory indicators (e.g., WBC count, CRP) and clinical assessment, rather than as a replacement for existing parameters. Its pertinent negative predictive value further indicates utility in ruling out infection. Larger cutoffs could be investigated in future experiments to improve specificity and rule-in performance. A two-threshold strategy (low cutoff for screening/rule-out and higher cutoff for confirmation/rule-in) may further increase therapeutic utility.

Distinguishing serious bacterial infections from viral illnesses in febrile children relies on clinical judgment, supported by evidence-based guidelines and relevant biomarkers. Routinely utilized traditional indices, such as WBC and ANC, demonstrate low diagnostic accuracy when used alone. In contrast, CRP and procalcitonin, despite their modest specificity and time-dependence, surpass WBC and ANC in identifying bacterial infections.[31] Blood cultures remain the gold standard for diagnosing serious bacterial infections [21], but due to limited pediatric sample volumes, delayed turnaround time, and suboptimal sensitivity for low-level pathogens, PCR-based molecular assays (multiplex/real-time) are now increasingly used in well-resourced settings.[32] These assays enable faster identification, higher sensitivity, and shorter turnaround times, enabling early commencement of treatment in high-risk cases.[33] Thus, rather than interpreting laboratory results separately, it is best to

interpret them in conjunction with a thorough clinical evaluation to maximize diagnostic accuracy in febrile children.

Our study assessed IG parameters as diagnostic markers for infection in a broad cohort of pediatric patients presenting with diverse aetiologies. The aim was timely identification of any infection, rather than focusing exclusively on sepsis or specific infection. This wider, inclusive approach parallels the real-world clinical practice in resource-constrained settings, where patients frequently present with a diverse range of infections. Our lower cutoffs align with the pediatric literature, favouring sensitive thresholds to enable early detection, and highlight clinical relevance of IG parameters across diverse aetiologies. Similar cut-offs have been reported such as; IG% cut-off of 0.25% and IG count of 0.03 × 10^6/mL for severe vesicoureteral reflux in pediatric UTI, 0.025 × 10^3/μL for relapse in pediatric nephrotic syndrome, 0.30% for PICU admission in RSV bronchiolitis and pediatric familial Mediterranean fever attacks (with concordant AUC of 0.891), 0.35% for SBI in children, post-treatment renal scarring in pediatric UTI or acute pyelonephritis, 0.45% for SBI prediction in Latvian pediatric cohorts, febrile UTI diagnosis in children and inflammation in children with pre-dialysis CKD (24, 34-37). Similarly, higher IG% and IG count, including measurements on day-3, were observed in non-survivors compared to survivors, comparable to our results, along with elevated APACHE II/SOFA scores and liver enzymes (18). Our study demonstrated higher AUC for IG parameters with more balanced sensitivity and moderate specificity. In contrast, Lee et al.'s [39] study on neutrophil-related indices in pediatric sepsis and SIRS demonstrated an AUC of 0.65 for IG count at a cut-off of 0.04 x 10^9/L (sensitivity 78.6%, specificity 48.1%, PPV 10.5%, and NPV 96.7%), and an AUC of 0.70 and 0.69 for delta neutrophil index parameters (DNI and DNII). These findings suggest that IG offered better overall discrimination for identifying pediatric infection. Ozcan et al demonstrated a concordant AUC of 0.891 and comparable IG% performance (cut-off 0.3%; sensitivity 81.3%, specificity 85.4%) in pediatric familial Mediterranean fever attacks; however, our specificity was lower in infection contexts.[35]

Similarly, the role of IG parameters in comparison with traditional CBC parameters has been supported by recent studies: In the studies by Güngör et al. 2021 (9), Gardovska et al. 2018 [36], and Nuran et al. 2023 (37), IG parameters outperformed WBC and ANC, which was similar to our results. The significant correlation of IG parameters with pediatric infection risk is further supported by odds ratios. In 2018, Pavare et al. found that for every 1% rise in IG%, the OR was 3.40 (95% CI 1.65–5.15) in children for serious bacterial infection (SBI) prediction in multivariable models(36). In pediatric SBI, Güngör et al. (2021) discovered that IG% was a powerful independent predictor, with an OR of 10.02 (95% CI 5.33–18.83, $p < 0.001$). [9] Cetin et al. (2023) found that children with UTIs had greater odds of developing renal scarring; HR (hazard ratio) 8.181 for IG count and HR 5.106 for IG% and OR 22.235 for IG count, OR 15.597 for IG% in severe vesicoureteral reflux [24]

In low- and middle-income countries (LMICs), IG parameters demonstrated lower cut-offs and higher sensitivity as a practical, affordable component of routine complete blood counts for early infection detection in settings of a high sepsis burden and limited diagnostic facility. Our study aligns with such trends; Senthilnayagam et al. (2012) in India reported moderate AUC (0.69 and 0.66), specificity >90% at higher thresholds (>0.3 ×109/L or >3%), and sensitivities of 88% and 96% at an absolute IG count >0.03 ×109/L and IG% >0.5% in febrile children (11). Similarly, in a study by Nguyen et al. (2025) in Vietnam, inclusion of IG parameters in the CBC model improved AUCs for IG (0.908 for septic shock) with better predictive performance than WBC and ANC alone in predicting septic shock and mortality in pediatric sepsis (38). According to Güngör et al. (2021) in Turkey, IG% sensitivity was 75.4% (cut-off >0.35%) with an AUC of 0.83.[9] In contrast, high-income countries reported high negative predictive value and relatively higher cut-offs for IG parameters. Lee et al. (2023) in Korea observed that an absolute IG count >0.04 ×10^9/L had a sensitivity of 78.6%, specificity of 48.1%, and a 96.7% NPV (AUC 0.65) in pediatric SIRS/sepsis. [39] Similarly, Pavare et al. (2018) from Latvia reported IG% sensitivity of 66% (cut-off >0.45%), with AUC of 0.80 (36). In Germany, Nierhaus et al. (2013) demonstrated IG count sensitivity of 89.2%, specificity of 76.4%, and AUC of up to 0.861 for early sepsis discriminating post-SIRS. [15]

Conclusion

This study shows that immature granulocyte parameters (IG% and IG count), derived from routine complete blood counts, outperform conventional leukocyte indices (WBC and ANC) and can help detect infections in febrile pediatric patients at their initial emergency department visit. With lower cut-offs for IG parameters (IG count 0.02 × 10^9/L and IG% cut-off 0.25%), offering balanced sensitivity and moderate specificity, and possessing independent predictive value, these parameters provide a quick, cost-effective adjunct marker alongside other parameters such as WBC, ANC and as a supplement to more expensive biomarkers like CRP and procalcitonin, enhancing early risk assessment, especially in resource-limited settings.

Strengths and limitations: The study established diagnostic thresholds for IG across various pediatric infections and provided baseline structured data for children admitted to hospitals with infections. However, it had some limitations. First, the research was conducted at a single tertiary care facility and focused on the hospital-pediatric population; the results may not be as applicable to other clinical settings with different patient groups, infection patterns, pathogen prevalences, or resource levels. Second, CRP, procalcitonin, and serological/molecular tests were not performed universally due to financial constraints. Since these labs were chosen based on clinical judgment, there may have been selection bias toward individuals with suspected serious infections or unclear diagnoses. Third, to establish baseline prediction performance against a healthy condition, we used clinically stable individuals with normal CBC as controls. Although this methodology is frequently used in early biomarker research (40), spectrum bias may cause it to overestimate diagnosis accuracy. Future research using viral or febrile non-infected comparators would be useful to assess IG performance in more clinically relevant situations. Fourth, only 116 of 150 patients had blood cultures, with 37.9% testing positive. The low overall positivity rate might be due to small sample sizes, prior antibiotic use, or fastidious microorganisms. This could have affected biomarker assessment and led to misclassification of some groups, such as culture-negative sepsis. Fifth, our research focused on general pediatric illnesses involving bacterial, viral, and other etiologies. Therefore, IG performance for broad infection prediction rather just bacterial infection or sepsis severity is reflected in the data. Although this may limit etiology-specific specificity, it more closely resembles pediatric practice in the real world, where prompt confirmation is frequently unavailable. Subgroup analyses should be used in future research. Lastly, the initial IG might have been affected by prior antibiotic use outside our hospital. Serial trends in immature granulocyte (IG) parameters were not analysed, so the study was limited to baseline laboratory data. Larger, multi-center studies with defined protocols and longitudinal assessments are needed to validate optimum cut-offs and examine their broader therapeutic value (41).

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