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Role of immature granulocytes in monitoring sepsis treatment

Mustafa Deniz[1*], Zahide Sahin Yildirim[2], Zuleyha Erdin[3], Murat Alisik[4], Ridvan Erdin[3] and Mustafa Yildirim[5]

Abstract

Background Sepsis is an organ dysfunction that impairs response to infection. Inflammatory biomarkers have been used to diagnose and monitor sepsis. The aim of the present study was to determine the role of immature granulocytes (IGs) in monitoring sepsis treatment.

Methods This two-center, prospective, observational study included patients diagnosed with sepsis according to the Sepsis-3 criteria, who were followed-up in the adult intensive care units of the Bolu Izzet Baysal State Hospital and Bolu Izzet Baysal Training and Research Hospital (Bolu Merkez/Bolu, Türkiye). Laboratory investigation results, demographic information, treatment responses, and mortality were recorded. Patients were divided into 2 groups according to treatment: appropriate (group 1); and inappropriate (group 2). Differences in the number of IGs and IG% were compared. Differences with $P < 0.05$ were considered to be statistically significant for all analyses.

Results The study included 87 patients from 2 centers. The most common comorbidities were hypertension (54%) and 28-day mortality (37.9%). Empirical antibiotic therapy (43.7%) was appropriate for 38 patients (group 1) and 49 patients when the treatment was incorrect or inadequate (group 2). There were no significant differences between the groups in terms of laboratory investigation results on the day of treatment initiation. IG count and IG% on day 3 of treatment were significantly higher in group 2. Mortality was higher in patients with a high IG count (IG %) and in group 2.

Conclusion IG% was a simple, inexpensive, and useful test for monitoring sepsis treatment and, in addition, IG count was also effective in predicting mortality.

Keywords Immature granulocytes, Sepsis, Treatment, Intensive care unit, Prognosis

Background

Sepsis is an organ dysfunction characterized by a dysregulated host response to infection(s) [1]. Although its associated mortality rate is high, early diagnosis and appropriate treatment can improve outcomes [2]. Diagnosis is made according to the Sepsis-3 criteria. Although biomarkers, such as procalcitonin (PCT), C-reactive protein (CRP), and interleukin (IL)-6, are helpful for diagnosis, they are relatively expensive tests and not always available [3]. When necessary, fluid resuscitation, vasopressors, source control, oxygenation, and early empirical antibiotic therapy are the main approaches to sepsis

*Correspondence:
Mustafa Deniz
drmdeniz@gmail.com
[1]Intensive Care Unit, Bolu Izzet Baysal State Hospital, Bolu, Turkey
[2]Department of Anesthesiology and Reanimation, Abant Izzet Baysal University Hospital, Bolu, Turkey
[3]Department of Internal Medicine, Abant Izzet Baysal University Hospital, Bolu, Turkey
[4]Medical Biochemistry, Bolu Abant Izzet Baysal University, Bolu, Turkey
[5]Department of Anesthesiology and Reanimation, Bolu Izzet Baysal State Hospital, Bolu, Turkey

management [4]. Excessive or incorrect use of empirical antibiotics, however, should be considered in terms of treatment optimization and the development of antibiotic resistance [3].

Immature granulocytes (IGs) are a subset of neutrophils (metamyelocytes, myelocytes, and promyelocytes), and are produced in the bone marrow prompted by stimuli such as inflammation or infection [5]. IGs are less mature cells than band cells and are usually present at lower levels. The ability to automatically determine percentage of IGs using modern analyzers enables faster and more precise measurement of left shift. Although many studies have been performed to determine the optimal cut-off value, there is no clear consensus [6].

As such, this study aimed to determine the role of IG% in predicting the response to microbiological treatment(s) for sepsis.

Methods

The present investigation was a two-center, prospective, observational study. Patients diagnosed with sepsis in the adult care units of the Bolu Izzet Baysal State Hospital and Bolu Izzet Baysal Training and Research Hospital (Bolu Merkez/Bolu, Türkiye) were followed up. Patients > 18 years of age, who were diagnosed with sepsis according to the Sepsis-3 criteria, were included in this study, which was approved by the Bolu Abant Izzet Baysal University Clinical Research Ethics Committee (Decision No.2023/314).

Variables such as age, sex, comorbidities, and Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scores, were recorded. Hemogram parameters, such as hemoglobin, white blood cell count, platelet count, IG count, and IG%, and biochemical parameters, such as albumin, bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, sodium, and potassium levels, were recorded on the day of diagnosis and antibiotic initiation. Inflammatory markers, such as PCT and CRP, vasoactive agent use, and mechanical ventilation requirements, were recorded at the time of diagnosis. Mortality status on day 28, hospital mortality status, and length of intensive care unit stay were recorded. Patients younger than 18 years, patients who were discharged from intensive care unit/died before 3 days, neutropenic and immunosuppressed patients were excluded.

The main aim of this study was to determine the role of IG% in predicting the response to antibiotic therapy in patients diagnosed with sepsis. When patients are diagnosed with sepsis, empirical antibiotic treatment is often initiated. If blood culture growth and antibiogram results are compatible with the antibiotherapy administered to the patient, empirical antibiotherapy is continued; if not, either the treatment strategy is altered or antibiotics are added to the regimen. Failure to improve hemodynamic and clinical deterioration or regression of inflammatory biomarkers requires a change in empirical antibiotherapy or switch to broad spectrum agents. Using defined variables, patients in whom empirical antibiotherapy was continued as "continuation of current treatment" were allocated to group 1, while those in whom antibiotics were changed or added 3–6 days after empirical treatment were allocated to the "group requiring treatment change" (group 2). Values measured on day 3 were used to predict treatment response. In the authors' hospitals, culture sample results are reported on day 6 at the latest. IG and IG% were measured on the day empirical antibiotic therapy was started and on day 3 of treatment using an automated hematology analyzer (XN1000, Sysmex Corporation, Kobe, Japan). IG% measured on day 3 was compared with that measured on the day of treatment initiation (IG% day 3/IG% day 1). In addition, IG% ratios were compared between the 2 groups.

An a priori power analysis was performed using G*Power 3.1.9.7 to determine the required sample size for comparing IG% between two independent groups. Based on the effect size (Cohen's d = 0.7) estimated from the study by Porizka et al(7). with a two-tailed alpha of 0.05 and power set at 0.90, the minimum required sample size was calculated as 38 participants per group (total $n = 76$).

Statistical analyses

All statistical analyses were performed using SPSS version 22 (IBM Corp., Armonk, NY, USA). Categorical variables are expressed as frequency and percentage, while continuous variables are expressed as mean ± standard deviation (SD) or median (interquartile range [IQR] i.e., Q1 to Q3]) depending on the normality of distribution, which was assessed using the Kolmogorov–Smirnov test. Comparisons between groups 1 and 2 were performed using the chi-squared test or Fisher's exact test for categorical variables, and the independent samples *t*-test or Mann–Whitney U test for continuous variables, as appropriate. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of IG%, IG% on days 0 and 3, and IG ratio for mortality. The area under the ROC curve (AUC) and corresponding 95% confidence interval (CI) for AUC, sensitivity, and specificity are reported. The optimal cut-off values were determined using the Youden index. Differences with $P < 0.05$ were considered to be statistically significant for all analyses.

Table 1 Demografics of patients

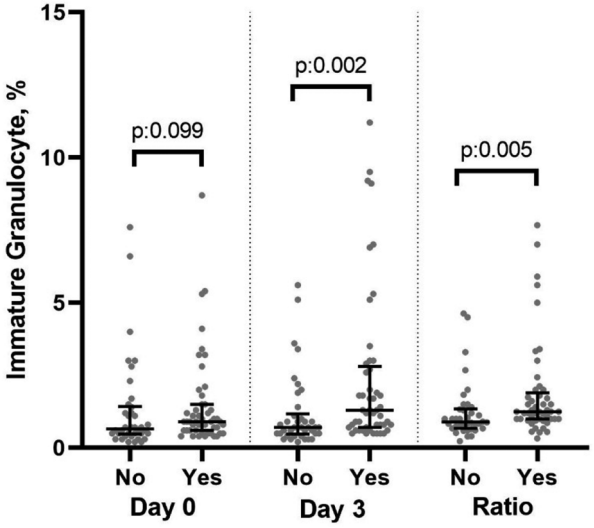
		***N*: 87 (%)**
Gender	Female	41 (%47.1)
	Male	46 (%52.9)
DM		28 (%32.2)
HT		47 (%54)
Cardiac disease		30 (%34.5)
COPD		20 (%23)
Malignancy		15 (%17.2)
CKD		11 (%12.6)
Neurologic disease		32 (%36.8)
Vasoactive drugs		42 (%48.3)
MV		66 (%76.9)
28. day mortality	live	54 (%62.1)
	dead	33 (%37.9)
Hospital mortality	discharged	41 (%47.1)
	dead	46 (%52.9)
AB changed	No	38 (%43.7)
	Yes	49 (%56.3)

DM: Diabetes Mellitus, HT: Hypertansion, COPD: chronic Obstructive Pulmonary Disease, CKD: Chronic Kidney Disease, MV: Mechanical Ventilation, AB changed: Empirical antibiotic changed

Table 2 APACHE LI, sofas and blood tests of groups

	Grup 1 (*N* = 38)	**Grup 2 (*N* = 49)**	***p* value**
Age	77 (63-82.3)	77 (66–85)	0.449
APACHE II	27.5 (24–31)	29 (25–32)	0.215
SOFAs	9.5 (7–11)	10 (7–12)	0.413
Hemoglobin (g/dL)	10.1 (8.9–12.2)	10 (8.8–12.1)	0.784
White blood cell (K/uL)	11.1 (8.5–16.3)	13.7 (10.1–19.8)	0.079
Platelets (K/uL)	228.5 (152.5-301.8)	239 (140–354)	0.584
Albumin (g/L)	29 (25-32.5)	28 (22.5–32.5)	0.479
Bilirubin (mg/dL)	0.7 (0.4–1.1)	0.5 (0.3–1.1)	0.261
Alanine amino transferase (U/L)	15.5 (11-45.8)	24 (14–57)	0.079
Aspartat amino transferase (U/L)	35 (18-60.8)	44 (22–76)	0.213
Creatinine (mg/dL)	1.1 (0.7–2.18)	1.2 (0.75–2.4)	0.575
Sodium (mmoL/L)	139 (135-144.3)	138 (136.5–142)	0.935
Potassium (mmoL/L)	4.25 (3.38–5.13)	4.2 (3.65–4.95)	0.942
Procalcitonin (µg/L)	0.6 (0.1–3.9)	1 (0.3–3.1)	0.613
C-Reactive Protein (mg/L)	97.5 (67–147)	140 (61-217.5)	0.06
IG%	0.65 (0.48–1.43)	0.9 (0.6–1.5)	0.099
IG% 3. day	0.7 (0.48–1.18)	1.3 (0.7–2.8)	**0.002**
IG ratio	0.89 (0.67–1.35)	1.25 (1-1.9)	**0.005**
IG count (10^9 /L)	0.08 (0.05–0.17)	0.13 (0.08–0.27)	**0.021**
IG count 3. day (10^9 /L)	0.06(0.04–0.15)	0.15(0.08–0.33)	**0.001**
Length of stay (day)	10 (7-25.8)	11 (7-28.5)	0.586

APACHE II: Acute Physiology and Chronic Health Evaluation II, SOFA s: Sequential Organ Failure Assessment score, IG: Immature granulocyte, IG Ratio: Immature granulocyte % day 3/ Immature granulocyte % day 0



Day 0: Immature granulocyte % on the day of empirical antibiotic initiation

Day 3: Immature granulocyte % on 3rd day of empirical antibiotic initiation

Ratio: Immature granulocyte % day 3/ Immature granulocyte % day 0

No: No change or addition of antibiotics

Yes: There is a change or addition of antibiotics

Fig. 1 Immature Granulocyte percentage, ratio and antibiotic change in 3–6 days status

Results

A total of 87 patients from 2 centers were included, and the data were prospectively analyzed. Empirical antibiotic treatment was continued in 38 patients, who comprised group (1) Forty-nine patients in whom empirical antibiotic treatment was changed or antibiotics were added within 3–6 days comprised group (2) Hypertension was the most common comorbidity ($n = 47$ [54%]), followed by neurological diseases ($n = 32$ [36.8%]), and cardiac diseases ($n = 30$ [30%]). At the time of diagnosis, 42 (48.3%) patients received vasoactive agent support and 66 (76.9%) received mechanical ventilator support. The 28-day and in-hospital mortality rates were 37.9% and 52.9%, respectively (Table 1).

When patients in group 1 and group 2 were compared according to the need for change(s) in antibiotic therapy, there was no significant difference between APACHE II, SOFA score, complete blood count/biochemical parameters, and inflammatory biomarkers in either group of patients with sepsis. The number of IGs at diagnosis was higher in group 2 ($P = 0.021$). The IG% at diagnosis did not differ between the groups. In blood samples collected on day 3 of treatment, the IG count ($P = 0.001$) and IG% ($P = 0.002$) were higher in group 2 than those in group 1. The ratio of IG% on day 3 after treatment initiation to IG% on the day of diagnosis (i.e., IG ratio) was also higher in group 2 ($P = 0.005$) (Table 2; Fig. 1).

The number of patients with malignancy was higher in group 2 ($P = 0.01$), as was the number of patients requiring mechanical ventilation support ($P = 0.003$). However, no significant differences were found between the groups in terms of other comorbidities and sex. The 28-day intensive care unit ($P = 0.049$) and hospital ($P = 0.008$) mortality rates were higher in group 2 (Table 3).

A binary logistic regression analysis was conducted to identify factors associated with antibiotic modification on day 7. The full model containing all predictors was statistically significant ($\chi^2 = 16.63$, df = 4, $p = 0.002$), indicating that the model reliably distinguished between patients who underwent antibiotic modification and those who did not. The model explained 23.3% of the variance (Nagelkerke $R^2 = 0.233$) and correctly classified 66.7% of cases, with a sensitivity of 81.6% and specificity of 47.4%. Among the variables included (IG%, malignancy, vasopressor use, and mechanical ventilation), malignancy (OR = 5.75, 95% CI: 1.12–29.53, $p = 0.036$) and mechanical ventilation (OR = 3.73, 95% CI: 1.20–11.54, $p = 0.022$) were statistically significant predictors of antibiotic modification. IG% and vasopressor use were not statistically significant predictors ($p > 0.05$). When discharge and intensive care unit mortality were analyzed, APACHE II and SOFA scores, ALT, AST, IG%, IG count, and IG count on day 3 were higher in the deceased patient group. Albumin levels were lower in patients who died ($P = 0.007$) (Table 4). When demographic data were compared, there were more patients with malignancy ($P = 0.012$) and ($p = 0.049$) higher mortality rate in group 2 (Table 5).

Logistic regression was performed to identify independent predictors of 28-day mortality. The overall model was statistically significant ($\chi^2 = 9.89$, $df = 4$, $p = 0.042$), indicating that the set of predictors reliably distinguished between survivors and non-survivors. The model explained approximately 14.6% of the variance in 28-day mortality (Nagelkerke $R^2 = 0.146$) and correctly classified 69.0% of cases, with a sensitivity of 36.4% and a specificity of 88.9%. Among the variables included in the model—IG%, presence of malignancy, vasopressor use, and mechanical ventilation—only the presence of malignancy was a statistically significant predictor of 28-day mortality (OR = 3.75, 95% CI: 1.09–12.84, $p = 0.036$). IG% showed a trend toward significance (OR = 1.31, 95% CI: 0.96–1.79, $p = 0.085$), while vasopressor use and mechanical ventilation were not statistically significant ($p = 0.756$ and $p = 0.737$, respectively). ROC analysis performed to define the adequacy of treatment yielded an AUC of 0.603 (95% CI: 0.479–0.727), a sensitivity of 0.653, and a specificity of 0.605 were found, with a cut-off value of 0.75 for IG% ($P = 0.099$). With a cut-off value of 0.75 for IG% on day 3, the AUC was 0.692 (95% CI:0.58–0.805), sensitivity was 0.735, and specificity was 0.579 ($P = 0.002$). For the

Table 3 Comorbidity, vasoactive drug use, mechanical ventilation support and prognosis of groups

		Grup 1. (*N* = 38) N(%)	Grup 2. (*N* = 49) N(%)	*p* value
Gender	Female	16 (42.1%)	25 (51%)	0.409
	Male	22 (57.9%)	24 (49%)	
DM		15 (39.5%)	13 (26.5%)	0.200
HT		23 (60.5%)	24 (49%)	0.284
Cardiac disease		17 (44.7%)	13 (26.5%)	0.076
COPD		10 (26.3%)	10 (20.4%)	0.516
Malignancy		2 (5.3%)	13 (26.5%)	**0.01**
CKD		6 (15.8%)	5 (10.2%)	0.437
Neurologic disease		16 (42.1%)	16 (32.7%)	0.364
Vasoactive drug		14 (36.8%)	28 (57.1%)	0.06
MV		23 (60.5%)	43 (87.8%)	**0.003**
28. day mortality	live	28 (73.7%)	26 (53.1%)	**0.049**
	dead	10 (26.3%)	23 (46.9%)	
Hospital mortality	discharged	24 (63.2%)	17 (34.7%)	**0.008**
	dead	14 (36.8%)	32 (65.3%)	

DM: Diabetes Mellitus, HT: Hypertansion, COPD: Chronic Obstructive Pulmonary Disease, CKD: Chronic Kidney Disease, MV: Mechanical Ventilation

Descriptives are presented as Number (percentage) (N(%)) and compared using the Mann-Whitney U or Chi-square tests respectively

Table 4 APACHE II, sofas, blood tests

	Discharged (*N* = 54)	Dead (*N* = 33)	*p* value
Age	77 (65-83.3)	77 (64.5–88.5)	0.584
APACHE II	27 (22.8–30.3)	31 (26–33)	**0.003**
SOFAs	9 (7–11)	10 (8.5–12)	**0.015**
Hemoglobin (g/dL)	10.35 (8.73–12.25)	10 (8.8–11.5)	0.674
White blood Cell (K/uL)	12.25 (8.9-17.75)	14.3 (8.85–21.2)	0.327
Platelets (K/uL)	237.5 (156.3-334.5)	210 (134–387)	0.776
Albumin (g/dL)	29.5 (25-34.8)	25 (21–31)	**0.007**
Bilirubin (mg/dL)	0.6 (0.3–1.1)	0.5 (0.4–1.1)	0.937
Alanine amino trasferase (U/L)	16.5 (12-38.3)	25 (17.5–85)	**0.027**
Aspartat amino transferase (U/L)	32.5 (18.8–54)	46 (30.5-142.5)	**0.014**
Creatinine (mg/dL)	1 (0.7–2.1)	1.6 (0.9–2.55)	0.057
Sodium (mmoL/L)	139 (136.8–142)	138 (136–145)	0.766
Potassium (mmoL/L)	4.4 (3.4–5.03)	4.1 (3.7-5)	0.934
Procalcitonin (µg/L)	0.45 (0.1–2.8)	1.7 (0.35–3.75)	0.059
C-Reactive Protein (mg/L)	122.5 (48.3-157.5)	144 (73.5–233)	0.192
IG %	0.7 (0.5–1.23)	0.9 (0.6–2.55)	**0.039**
IG 3. day %	0.85 (0.58–1.5)	1.3 (0.6–3.45)	0.072
IG ratio	1.09 (0.83–1.5)	1.09 (0.83–1.9)	0.707
IG count (10^9 /L)	0.09 (0.05–0.15)	0.18 (0.07–0.34)	**0.033**
IG count 3. day (10^9 /L)	0.08 (0.04–0.19)	0.16 (0.07–0.39)	**0.014**

APACHE II: Acute Physiology and Chronic Health Evaluation II, SOFA s: Sequential Organ Failure Assessment score, IG: Immature granulocyte, IG Ratio: Immature granulocyte % day 3/ Immature granulocyte % day 0

Table 5 Demographics, MV, and vasoactive use differences between dead and discharged patients

		Discharged *N*:54(%)	Dead *N*:33(%)	
Gender	Female	30 (55.6%)	11 (33.3%)	**0.044**
	Male	24 (44.4%)	22 (66.7%)	
DM		19 (35.2%)	9 (27.3%)	0.443
HT		32 (59.3%)	15 (45.5%)	0.210
Cardiac disease		22 (40.7%)	8 (24.2%)	0.116
COPD		11 (20.4%)	9 (27.3%)	0.458
Malignancy		5 (9.3%)	10 (30.3%)	**0.012**
CKD		7 (13%)	4 (12.1%)	0.909
Neurologic disease		23 (42.6%)	9 (27.3%)	0.150
Vasoactive drugs		26 (48.1%)	16 (48.5%)	0.979
MV		39 (72.2%)	27 (81.8%)	0.310
AB changed		26 (48.1%)	23 (69.7%)	**0.049**

DM: Diabetes Mellitus, HT: Hypertansion, COPD: chronic Obstructive Pulmonary Disease, CKD: Chronic Kidney Disease, MV: Mechanical Ventilation, AB changed: Empirical antibiotic changed

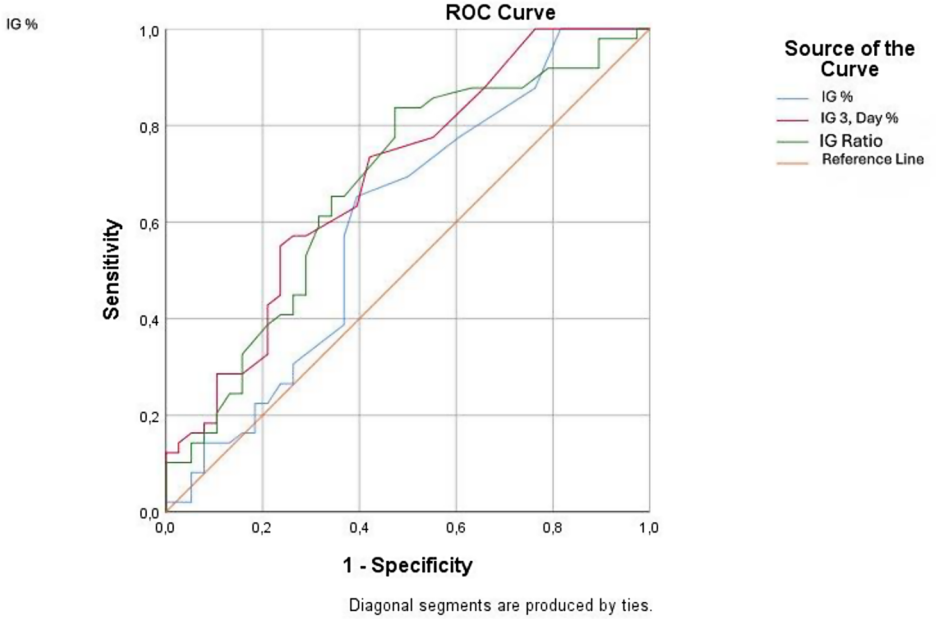
Descriptives are presented as Number (percentage) (N(%)) and compared using the Mann-Whitney U or Chi-square tests respectively

IG ratio, the AUC was 0.676 (95% CI: 0.56–0.791)), sensitivity was 0.837, and specificity was 0.526 ($P = 0.005$), with a cut-off value of 0.915 (Fig. 2).

Discussion

Biomarkers are useful to diagnose, monitor treatment response, and predict prognosis of sepsis or suspected sepsis. Biomarkers must be highly specific, sensitive, reproducible and cost effective [7]. Many biomarkers have been investigated for their role in differentiating conditions such as infection, trauma, surgery, malignancy, and ischemia [8]. The IG count and IG% have recently been investigated for their roles in reflecting infection status.

Yazla et al. [9] found that IG count and IG% were significant biomarkers for predicting the diagnosis of complicated acute appendicitis in patients undergoing surgery for acute appendicitis. In a similar study, Durak et al. [10] reported that IG count was an effective biomarker for predicting mesenteric ischemia and intestinal necrosis in patients undergoing laparotomy. Porizka et al. [11] reported that IG% could be used to differentiate between infective and non-infective systemic inflammatory response syndromes (i.e.,"SIRS") in patients undergoing cardiac surgery. Jeon et al. [12] evaluated the IG% to be moderately effective in predicting sepsis in patients with burns and recommended it as an auxiliary test due to its cost and ease of routine use. They reported that IGs



	Cut-off	AUC (95% CI)	p value	Sensitivity	Specificity
IG%	**0.75**	0.603 (0.479-0.727)	0.099	0.653	0.605
IG% day 3,	**0.75**	0.692 (0.58-0.805)	0.002	0.735	0.579
Ratio	**0.915**	0.676 (0.56-0.791)	0.005	0.837	0.526

AUC (95% CI) :Area under curve (95% Confidence interval) IG%: Immature granulocyte % on the day of empirical antibiotic initiation, IG% day 3: Immature granulocyte % on 3th day of empirical antibiotic initiation, Ratio: Immature granulocyte % day 3/ Immature granulocyte % day 0

Fig. 2 ROC curves of IG % and IG ratios in predicting antibiotic changing status

were effective markers for differentiating bacterial pneumonia in patients with severe acute respiratory syndrome coronavirus 2 (i.e., "SARS-CoV-2") infection [13].

In a study conducted in a non-septic intensive care unit, blood tests were performed for 7 days, and the IG count and IG% were found to have high sensitivity and specificity in the early recognition of sepsis [3]. In a similar study, IG% was defined as a useful and effective marker of the development of infections and septic shock [14]. Ayres et al. [15] found that a low IG% demonstrated high specificity in excluding sepsis and reported that it was a useful additional marker. In a study comparing blood culture-positive groups, IG% was found to be effective for the early detection of bacteremia [16]. Although the IG count and IG% have supported the diagnosis of sepsis in previous studies, there has been heterogeneity in some results [17].

The half-life of IGs is 3 h, and the capacity of this marker to better reflect the state of inflammation compared with other markers with long half-lives is remarkable [18]. In our study, blood samples collected on the day of the empirical treatment were analyzed. There was no significant difference in PCT and CRP levels between the groups in which empirical treatment was appropriate and a response to treatment was obtained (i.e., group 1) and the group in which empirical treatment was inadequate (i.e., group 2). Again, there was no significant difference in IG% on the day of treatment initiation in either group. In blood samples obtained on day 3 of empirical treatment, IG% was significantly higher in the group in which antibiotics were added due to inadequate empirical treatment or antibiotic therapy was changed according to the culture results. When we compared IG% on day 3 with IG% on the day of treatment initiation, this ratio was significantly higher in the inadequate treatment group (group 2) than in the adequate treatment group (group 1). When we analyzed the number of IGs, the mean number of IGs decreased on day 3 in the adequate treatment group, whereas the mean number of IGs increased in the inadequate treatment group.

In reviewing the literature, IG% and IG counts have been investigated in terms of diagnosis and prognosis of sepsis. However, it attracted our attention that the power of this hemogram parameter, which is inexpensive, easy to measure and useful, in monitoring the response to treatment has not been investigated. Our results encouraged us to investigate their roles in treatment monitoring. We believe that IG% and IG count, which are inexpensive and useful parameters, may be effective at follow-up, although further studies are required.

In group 2, the 28-day and hospital mortality rates were significantly higher. Again, when we compared patients who were discharged with those who were deceased, mortality was higher in the group in which antibiotics were changed; more specifically, in which treatment was inadequate. In this context, we agree that antibiotic treatment and follow-up are especially important for sepsis. The IG% and the number of IGs were higher on the day of treatment initiation and on day 3. Similar to most studies, we believe that IG% and IG counts are effective predictors of mortality.

Our study had several limitations. First, although this was a two-center study, the sample size was relatively small. The treatment of sepsis is a multidisciplinary approach, and we may not have standardized fluid therapy, doses of inotropes and vasoactive agents, corticosteroid support, mechanical ventilation modes and pressures, or nutritional status.

In conclusion, patients treated for sepsis either recover or die. In situations in which antibiotic therapy, fluid therapy, and vasoactive agent support are involved, we believe that IG% and IG count are inexpensive, and useful hemogram parameters for monitoring the bacteriological treatment of sepsis. IG% may be a potential follow-up marker; however, it should be assessed alongside other clinical parameters in the decision-making process. We believe that additional studies should be performed to fill this knowledge gap in the literature.

Abbreviations

ALT	Alanine aminotransferase
APACHE	Acute Physiologic Assessment and Chronic Health Evaluation
AST	Aspartate aminotransferase
CRP	C-Reactive Protein
IG	Immature Granulocytes
IL	Interleukin
PCT	Procalcitonin
SOFA	Sequential Organ Failure Assessment

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Author contributions

MD, ZSY, ZE, RE, MA and MY equally contributed to the conception and design of the research. MD, ZSY, MA, RE, ZE and MY contributed to the acquisition of the data. MD, ZSY, MA, ZE, RE and MY contributed to the analysis and interpretation of the data. MD, ZSY, ZE, RE, MA and MY drafted the manuscript. All authors read and approved the final manuscript.

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Data availability

The data are recorded in the automation system of the hospital where the study was conducted and in the study participants. It can be shared with the relevant authorities upon request.

Declarations

Ethics approval and consent to participate

The Bolu Abant İzzet Baysal University Clinical Research Ethics Committee approved this study with the ethical code 2023/314. Written informed consent was received from all subjects or their care givers before beginning the study. All methods were carried out in accordance with relevant guidelines and regulations or Declaration of Helsinki.

Competing interests
The authors declare no competing interests.

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