

Diagnostic test of Immature Granulocyte Ratio (IG Ratio) to detect Early-Onset Neonatal Sepsis (EONS)



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ABSTRACT

Background: Based on the onset of events, the most common neonatal sepsis is early-onset neonatal sepsis (EONS), which occurs within the first 72 hours of life. Blood culture is the gold standard for EONS, but this examination takes a long time to provide the results. However, the latest method is obtained to determine the shift to the left granulocytic image by counting Immature Granulocyte (IG). This study aims to evaluate the accuracy of the IG Ratio for diagnosing EONS in neonates suspected of having sepsis.

Methods: A cross-sectional observational study was conducted among 60 EONS patients consecutively, who met the inclusion criteria from January to June 2022 at Prof. dr. I.G.N.G Ngoerah Hospital, Bali. Variables assessed in this study included age, gender, delivery methods, birth status, birthweight, blood culture, complete blood count (CBC), I/T ratio, and IG ratio. Data were analyzed using SPSS version 23 for Windows.

Results: The cut-off point of the IG Ratio was 2.21 (AUC=0.670 (0,490-0,851); p=0.041; OR: 8.021 (2.283-28.185); p=0.001), which had a sensitivity of 64.7% and a specificity of 81.4% for diagnosing EONS in neonates suspected of having sepsis. The results also obtained a Negative Predictive Value (NPV) of 85.35 and a Positive Predictive Value (PPV) of 57.89.

Conclusion: The cut-off point of the IG Ratio of 2.21 has a risk factor of 8.021 times higher for diagnosing EONS in neonates with sepsis.

Keywords: Immature Granulocyte Ratio, Diagnostic Test, EONS.

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INTRODUCTION

Early Onset Neonatal Sepsis (EONS) is an event in the first 72 hours of life that can be caused by vertical infection from the mother with a mortality rate of 5-20%.¹ The most common organism in developing countries is *Klebsiella pneumoniae*, followed by *Staphylococcus aureus* and *Pseudomonas*. The sepsis condition can occur during antenatal, intranatal and postpartum.² Data on the etiology and incidence of EONS in Indonesia as a whole still do not exist, but based on data at Prof. dr. I.G.N.G Ngoerah Hospital Denpasar related to Late-Onset Neonatal Sepsis (LONS) in 54 subjects, indicating that sepsis often occurs due to premature infant age.³

Diagnosis and early detection of sepsis should be conducted as soon as possible

to provide the best prognosis. Blood culture is the gold standard, but the results are only obtained after 48-72 hours and are influenced by antibiotics obtained during delivery, only 30-40% give positive results.⁴ Examination with blood culture takes a long time, so it is not suitable to be able to diagnose EONS cases.⁵ Several other parameters that can be used to diagnose neonatal sepsis are: shift to the left, Immature Granulocyte Ratio (IG Ratio), Hematology Scoring System (HSS), Immature-to-Total Neutrophil (IT) ratio, and procalcitonin.^{6,7}

There is a new method to determine the shift to the left granulocytic by counting immature granulocytes (IG). The part that includes IG includes promyelocytes, myelocytes, and metamyelocytes formed by bone marrow progenitor cells and will undergo maturation into neutrophils. At

the time of sepsis, IG can be found to be elevated due to low levels of granulocytes, so the bone marrow releases young granulocytes into circulation.⁸ IG calculation can be seen from immature granulocyte absolute (IG#), immature granulocyte percentage (IG%) and immature granulocyte ratio (IG Ratio).⁸ Calculate the IG Ratio using the formula IG# divided by total white blood cells (WBC), then multiply by 100. Examination of immature granulocyte absolute (IG#) can be calculated by multiplying the total white blood cell (WBC) total by the percentage of granulocytes.⁸ Studies related to the calculation of the IG Ratio have not been carried out on blood samples from newborns. Still, a study conducted by Iddles C et al., explained that the IG ratio threshold of 0.35 has a sensitivity of 74% and a specificity of 35% for diagnosing

sepsis in patients who are in intensive care rooms.⁹ The study also reported that the IG Ratio was more accurate in detecting sepsis than CRP.⁹ A similar study by Noviani I et al., also concluded that the IG Ratio could be used as a predictor of infection and sepsis because the results of the IG Ratio calculation are higher in patients with bacterial infections with positive blood culture results.¹⁰ Therefore, the IG Ratio is a better predictor of infection than the number of leukocytes based on the previous studies.^{9,10}

Based on those mentioned above, this study aims to assess the diagnostic ability of immature granulocyte ratio (IG Ratio) in EONS patients at Prof. dr. I.G.N.G Ngoerah Hospital, Denpasar.

METHODS

This study is an observational study with a diagnostic test using a cross-sectional approach on 60 EONS patients at Prof. RSUP. dr. I.G.N.G Ngoerah, Denpasar, Bali using a consecutive sampling method. Inclusion criteria in this study included: 1) Neonates with EONS or neonatal sepsis occurring within the first 72 hours after birth; 2) Parents allow their children to be research samples by signing the PSP that has been provided; and 3) Have complete medical record data according to the desired variable. While the exclusion criteria in this study include: 1) Hematological malignancy (Leukemia); 2) Neonates receiving blood transfusions; 3) Hemolytic Disease of the Newborn (HDN); and 4) genetic disorders (Down syndrome).

Immature Granulocyte ratio (IG Ratio) is a calculation of IG absolute (IG#) divided by the total number of leukocytes and then multiplied by 100. Examination of Immature Granulocyte (IG) includes promyelocytes, myelocytes, and metamyelocytes formed by bone marrow progenitor cells and will undergo maturation into neutrophils. The results of the calculation of the IG Ratio were measured using the Hematology Analyzer Sysmex XN-3000 from the K2-EDTA vein sample that had undergone Internal Quality Control using Westgard Multirule analysis. Blood culture examination showed positive results if there was bacterial growth while negative if there was

no growth of bacteria or microorganisms causing infection using the BacT/ALERT Microbial Detection System. Neonates with Early Onset Neonatal Sepsis (EONS) are diagnosed by the doctor in charge of the patient if there are risk factors for infection (at least 1 risk for major infection or 2 risks for minor infection) accompanied by clinical examination and physical examination, as well as abnormalities in at least 2 laboratory tests with or without positive blood culture results.

The data from this study were statistically analyzed with the help of the IBM SPSS version 23 program for Windows. Descriptive analysis was carried out, including a normality test using Kolmogorov-Smirnov, where normal data distribution will be presented in the form of mean \pm standard deviation (SD). In contrast, numerical variables with abnormal distribution will be presented as the median and interquartile range (IQR). Categorical variables will be presented as a frequency table with absolute numbers and percentages. ROC analysis was carried out to assess the ability of the IG ratio to predict the diagnosis of EONS and to find the optimal IG ratio cut-off point for predicting the diagnosis of EONS in neonates. This analysis also includes sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and accuracy. The p-value is said to be significant if it is less than 0.05.

RESULTS

The results showed that most of the patients aged 1.00 (1.00-3.00) days, accompanied by the number of females more than the number of males, namely 32 females (53.30%) and 28 males (46.70%). The method of delivery of EONS patients with cesarean section was 51 patients (85.00%) and 9 patients (15.00%) vaginally. The birth status of EONS patients was more preterm with 51 patients (85.00%) than aterm 9 patients (15.00%). Based on birth weight, EONS patients were divided into 3 groups such as normal birth weight 13 patients (21.70%), low birth weight (<2500 grams) 33 patients (55.00%), and very low birth weight (< 1500 grams) 14 patients (23.30%). In EONS patients, blood cultures were also examined with positive culture results in as many as 17 people

(28.30%) (Table 1).

Based on Table 2, it can be seen that the sample characteristics from positive culture results with the most species, namely *Staphylococcus coagulase* negative in samples (47%), *Klebsiella pneumoniae* in 3 samples (17.64%), *Candida parapsilosis* in 2 samples (11.76%), *Enterobacter cloacae* in 1 sample (5.88%), *Acinetobacter lwoffii* in 1 sample (5.88%), *Streptococcus dysgalactiae ssp. dysgalactiae cloacae* in 1 sample (5.88%), and *Staphylococcus haemolyticus* in 1 sample (5.88%).

The number of leukocytes obtained a median value was 13.13 (2.55-46.13) $\times 10^3/\mu\text{L}$, followed by absolute neutrophil count (6.49 (0.71-31.94) $\times 10^3/\mu\text{L}$), neutrophil percentage (56,15 (18.70-88.40)%), platelet count (246.13 \pm 100.51 $\times 10^3/\mu\text{L}$), procalcitonin (0.21 (0.01-134) ng/ml), Immature to Total neutrophil Ratio (I/T ratio) (0.09 (0.03-0.29)), Immature Granulocyte (IG) Absolute (0.18 (0.01-6.27) $\times 10^3/\mu\text{L}$), IG percentage (1.30 (0.20-13.60)%), and IG Ratio (1.32 (0.07-13.59)) (Table 3).

The analysis results showed significant differences in gender, leukocyte count, absolute IG, IG Percentage, and IG Ratio in the positive culture EONS group compared to the negative culture EONS group using the Mann-Whitney U test, Fisher Exact Test and Independent T-Test. ($p < 0.05$) (Table 4).

Figure 1 shows the Area Under Curve (AUC) analysis of the Receiver Operating Curve (ROC) for the IG Ratio is 0.670 ($p = 0.041$). The cut-off point for the IG Ratio in patients with early-onset neonatal sepsis (EONS) was 2.21, followed by IG Percentage (3.20) and Absolute IG (0.34). The sensitivity of IG Ratio, IG Percentage, and Absolute IG is 64.7%, respectively; 47.1%; and 64.7%. The highest specificity result was IG Percentage which was 86.0%, followed by IG Ratio and Absolute IG, each of 81.4% ($p < 0.05$) (Table 5).

In Table 6, a bivariate analysis of risk factors for early-onset neonatal sepsis (EONS) was performed with positive cultures for Immature Granulocyte (IG), namely IG Ratio, IG Percentage, and Absolute IG using the Chi-Square test. The results of the IG Ratio analysis showed that the NPV value was 85.35 and the PPV was 57.89 (OR=8.021) ($p = 0.001$).

Table 1. Baseline characteristics of respondents.

Parameter	Total (N=60)
Age (Days), Median (Min-Max)	1.00 (1.00-3.00)
Gender, n (%)	
Male	28 (46.70)
Female	32 (53.30)
Delivery Methods, n (%)	
Cesarean section	51 (85.00)
Vaginally	9 (15.00)
Birth Status, n (%)	
Preterm	51 (85.90)
Aterm	9 (15.00)
Birthweight, n (%)	
Normal	13 (21.70)
LBW	33 (55.00)
VLBW	14 (23.30)
Blood Culture, n (%)	
Positive	17 (28.30)
Negative (No Growth)	43 (71.70)

Min: Minimum; Max: Maximum; LBW: Low Birth Weight; VLBW: Very Low Birth Weight

Table 2. Species distribution based on the culture-positive results.

Species	N=17
<i>Staphylococcus coagulase negative</i> , n (%)	8 (47.5)
<i>Enterobacter cloacae</i> , n (%)	1 (5.88)
<i>Klebsiella pneumoniae</i> , n (%)	3 (17.64)
<i>Candida parapsilosis</i> , n (%)	2 (11.76)
<i>Acinetobacter lwoffii</i> , n (%)	1 (5.88)
<i>Streptococcus dysgalactiae ssp. dysgalactiae</i> , n (%)	1 (5.88)
<i>Staphylococcus haemolyticus</i> , n (%)	1 (5.88)

Table 3. Characteristics of research participants based on the results of laboratory examinations.

Parameter	Total (N=60)
Leukocytes (10 ³ /μL), Median (Min-Max)	13.13 (2.55-46.13)
Neutrophils (10 ³ /μL), Median (Min-Max)	6.49 (0.71-31.94)
Neutrophils (%), Median (Min-Max)	56.15 (18.70-88.40)
Platelet (10 ³ /μL) (Mean±SD)	246.13±100.51
Procalcitonin (ng/ml), Median (Min-Max)	0.21 (0.01-134.00)
I/T ratio, Median (Min-Max)	0.09 (0.03-0.29)
IG absolute (10 ³ /μL), Median (Min-Max)	0.18 (0.01-6.27)
IG percentage (%), Median (Min-Max)	1.30 (0.20-13.60)
IG ratio, Median (Min-Max)	1.32 (0.07-13.59)

IG: Immature Granulocyte; IG Ratio: Immature Granulocyte Ratio; I/T Ratio: Immature to Total neutrophil Ratio; Min: Minimum; Max: Maximum; SD: Standard Deviations

IG percentage analysis obtained the NPV value of 80.43 and PPV of 57.14 (OR=5.481) (p=0.006). The results of the IG absolute analysis showed that the NPV value was 85.35 and the PPV was 57.89 (OR=8.021) (p=0.001). This study's Odds Ratio (OR) Immature Granulocyte Ratio (IG Ratio) was 8.021. Thus the group of culture-positive EONS patients with an IG Ratio greater than 2.21 had a risk factor of 8.021 times higher for the incidence of

EONS (Table 6).

DISCUSSION

The proportion of delivery methods in this study was the method of delivery by cesarean section. This is in accordance with a previous study for neonatal sepsis, which is more common in infants with surgical delivery processes (Section Caesarea, vacuum extraction, forceps

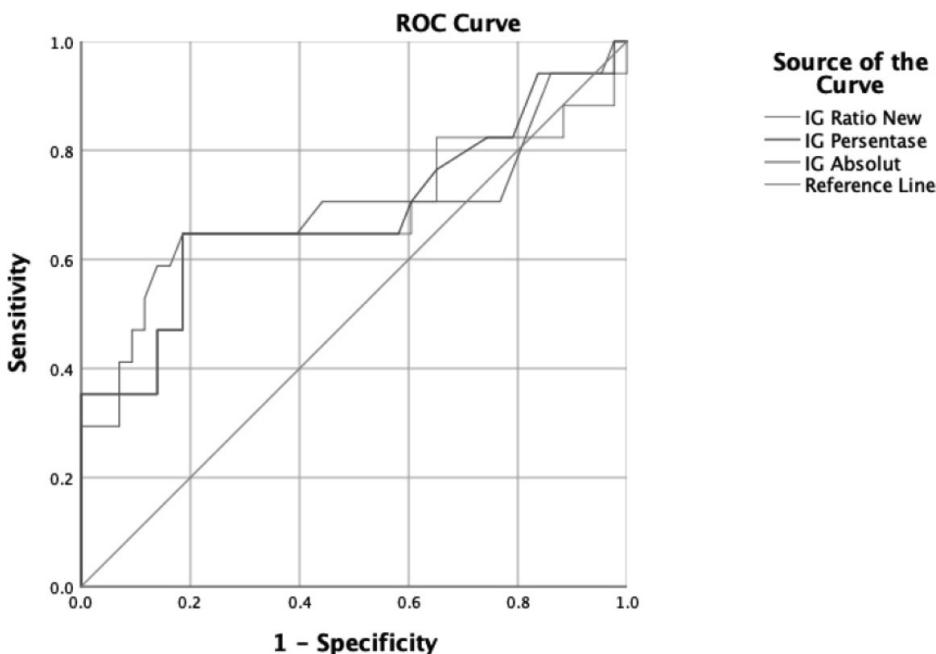
extraction,) which may be due to bacterial contamination of birthing aids.¹¹ However, transmitting pathogens from the mother during spontaneous delivery is also important, especially in women with premature rupture of membranes and urinary tract infections.¹¹

In this study, it was shown that the age of the baby was born at a gestational age of less than 37 weeks (preterm). The proportion of premature (preterm) and full-term (term) infants differed significantly between preterm (85%) and term (15%). Then, the highest proportion of low birth weight (LBW) babies was 55%. These results align with previous studies that premature and low birth weight infants dominate infants with neonatal sepsis.^{12,13} Premature and low birth weight conditions are associated with sepsis caused by an immature immune system, so babies are more at risk of infection. Premature babies have several conditions related to immaturity.^{12,13} The respiratory center regulation is not perfect and the respiratory muscles and os costae are still not too strong, so the oxygen that enters the brain is inadequate. Lack of oxygen entering the brain causes anaerobic bacteria to grow easily, causing infection in the baby. Another study also stated that the proportion of infants with neonatal sepsis was more likely to be born prematurely than at term, which was caused by an immature immune system, namely lower serum immunoglobulin levels, skin conditions that are more vulnerable. as a primary defense, secretory function of IgA in the immature intestinal mucosa as a protective layer against the bacterial invasion of the digestive system and also the function of an imperfect adaptive response.^{12,13} In addition, neutrophils, macrophages and T lymphocytes that play an important role in fighting infection are not fully developed. They cannot carry out a complete inflammatory response in neonates during infection. LBW conditions are associated with neonatal sepsis because LBW can lose weight at any time, in contrast to babies born with a normal weight, where weight loss usually occurs in the first week and the following week, there is an increase in body weight. The lower the baby's birth weight, the higher the risk of developing sepsis.¹²⁻¹⁴

Table 4. The relationship between several variables in the EONS group.

Parameter	EONS Culture (N=60)		P
	Positive (N=17)	Negative (N=43)	
Age (Days), Median (Min-Max)	1.00 (1.00-2.00)	1.00 (1.00-3.00)	0.271 ^a
Gender, n (%)			
Male	2 (11.80)	26 (60.50)	0.001 ^{b*}
Female	15 (88.20)	17 (39.50)	
Delivery Methods, n (%)			
Cesarean section	15 (88.20)	36 (83.70)	1.000 ^b
Vaginally	2 (11.80)	7 (16.30)	
Birth Status, n (%)			
Preterm	15 (88.20)	36 (83.70)	1.000 ^b
Aterm	2 (11.80)	7 (16.30)	
Birthweight, n (%)			
Normal	1 (5.90)	12 (27.90)	-
LBW	6 (35.30)	27 (62.80)	
VLBW	10 (58.80)	4 (9.30)	
Leukocytes (10 ³ /μL) (Mean±SD)	20.03±10.38	12.49±4.85	0.010 ^{c*}
IG absolute (10 ³ /μL), Median (Min-Max)	0.47 (0.02-6.27)	0.14 (0.01-0.85)	0.023 ^{a*}
IG percentage (%), Median (Min-Max)	2.50 (0.30-13.60)	1.30 (0.20-5.20)	0.027 ^{a*}
IG ratio, Median (Min-Max)	2.54 (0.07-13.59)	1.28 (0.15-5.17)	0.041 ^{a*}

LBW: Low Birth Weight; VLBW: Very Low Birth Weight; Min: Minimum; Max: Maximum; IG: *Immature Granulocyte*; ^aMann-Whitney U; ^bFisher Exact Test; ^cIndependent T-Test; *Statistically significant if p-value less than 0.05.

**Figure 1.** ROC analysis of *Immature Granulocyte* (IG).

Various germs, such as bacteria, viruses, parasites, or fungi can cause infection. The pattern of germs that cause sepsis differs between countries and always changes from time to time. Even in developing countries, differences in bacterial patterns are found, although gram-negative bacteria are the main cause of neonatal sepsis. In this study, the most species found were *Staphylococcus coagulase negative*.¹⁵ *Staphylococcus coagulase negative* has been

reported as the most common cause of early-onset neonatal sepsis. These bacteria cause bacteremia associated with the use of indwelling devices. *Staphylococcus coagulase negative* is normal flora on the skin. However, in another study, group B Streptococcus sp (GBS) and Gram-negative organisms (*Escherichia coli* and *Klebsiella pneumonia*) were the most common dominant pathogens.¹⁵

In this study, the procalcitonin levels

obtained a median value of 0.21 ng/ml with a minimum value of 0.01 ng/ml and a maximum value of 134 ng/ml. Almost similar results were obtained in the study of Li T et al., in 2022, from 758 neonates with a diagnosis of sepsis obtained a median procalcitonin 0.32 (0.14-1.52) ng/mL where procalcitonin levels were high in neonates with sepsis.¹⁶ Habib A et al., in 2021 also found that of 171 neonates with clinical sepsis, the median procalcitonin was 1.51 (0.32-10.28) ng/mL.¹⁷ Another study conducted by Morad EA et al., in 2020 in clinical sepsis patients obtained a median PCT value of 10.4 (0.1-50.6) ng/mL.¹⁸

Immature to Total neutrophil Ratio (I/T ratio) obtained a median value of 0.09 with a minimum value of 0.03 and a maximum value of 0.29. A shift-to-the left of the leukocyte count with an increase in immature neutrophils is common in patients with neonatal sepsis due to bacteria. A previous study has shown that the Immature to Total neutrophil Ratio (I/T ratio) > 0.2 indicates an abnormality which indicates that the sepsis process is ongoing.¹⁹

The absolute number of Immature Granulocyte (IG) obtained a median value of 0.18x10³/μL with a minimum value of 0.01x10³/μL and a maximum value of 6.27x10³/μL. The IG Ratio parameter can describe the possibility of a response

Table 5. Receiver Operating Curve (ROC) analysis of Immature Granulocyte in EONS.

Groups	AUC	95%CI	Cut-Off	Sensitivity (%)	Specificity (%)	p
IG Ratio	0,670	0,490-0,851	2,21	64,7	81,4	0,041*
IG Percentage	0,685	0,513-0,856	3,20	47,1	86,0	0,027*
IG Absolute	0,689	0,510-0,867	0,34	64,7	81,4	0,024*

AUC: Area Under Curve; IG: Immature Granulocyte; *Statistically significant if p-value less than 0.05.

Table 6. Bivariate analysis of EONS with positive culture to the Immature Granulocyte (IG).

Variable	EONS (N=60)		NPV (%)	PPV (%)	OR	95% CI		P
	Culture (+) (N=17)	Culture (-) (N=43)				Lower	Upper	
IG Ratio, n (%)								
≥2.21	11 (64.70)	8 (18.60)	85.35	57.89	8.021	2.283	28.185	0.001*
< 2.21	6 (35.30)	35 (81.40)						
IG Percentage, n (%)								
≥3.20	8 (47.10)	6 (14.00)	80.43	57.14	5.481	1.517	19.813	0.006*
< 3.20	9 (52.90)	37 (86.00)						
IG Absolute, n (%)								
≥0.34	11 (64.70)	8 (18.60)	85.35	57.89	8.021	2.283	28.185	0.001*
< 0.34	6 (35.30)	35 (81.40)						

EONS: Early Onset Neonatal Sepsis Dini; IG: Immature Granulocyte; NPV: Negative Predictive Value; PPV: Positive Predictive Value; OR: Odd Ratio; Chi-Square-Test: *Statistically significant if p-value less than 0.05.

to acute infection in the early phase, where clinical parameters and other hematological parameters are still within normal limits.²⁰ Research conducted by Nigro KG et al., showed the equivalence of the predictive ability of neonatal sepsis based on the IG Ratio, which was examined by traditional manual type counting and automatic hematology tools.²⁰

The analysis results showed significant differences in sex, leukocyte count, IG absolute, IG percentage, and IG ratio in the positive culture EONS group compared to the negative culture EONS group ($p < 0.05$). Another study reported other risk factors associated with sepsis in neonates. The male sex is four times more likely to be infected than the female, giving unhygienic food and drink to the mother and low socioeconomic status because it can cause low birth weight.²¹ The ratio of sepsis between men and women is 1.1:1. This result is almost the same as the study at Cipto Mangunkusumo Hospital in Jakarta, which found the ratio of neonatal sepsis between men and women was 1.25:1.²¹ In another study, it was found that male infants experienced neonatal sepsis more often, such as at Prof. dr. I.G.N.G Ngoerah Hospital Denpasar, 56.8% males were found out of 125 septic neonates treated.²² One hypothesis explains this difference because the factors that regulate

immunoglobulin synthesis may be on the X-chromosome; therefore, the presence of two chromosomes in females results in a greater defense function against infection.^{21,22}

The results of Immature Granulocyte (IG) and IG percentage using the Mann-Whitney U test in both groups of positive culture EONS and negative culture EONS showed significant results ($p < 0.05$). Clinical factors affecting the IG examination are asphyxia, hematological malignancies such as Chronic Myeloid Leukemia (CML), Hemolytic Disease of the Newborn (HDN), and neonates with Down syndrome. Antibiotics also reduce the possibility of positive culture because it has a bactericidal or bacteriostatic effect that inhibits bacterial growth. Administration of low-dose steroids in neonatal sepsis can reduce the systemic inflammatory response, as a vasopressor, inhibit the production of proinflammatory cytokines, inhibit the production of inflammatory mediators such as cyclooxygenase-2, reduce leukocyte adhesion to the endothelium so that the amount of IG decreases.²³ The results of IG Absolute, IG Percentage and IG Ratio in this study are similar to those obtained in the study of Cimenti C et al., namely significant differences in IG Absolute, IG Percentage and IG Ratio, which showed

that a significantly higher percentage of IG was found in neonates with EONS compared to neonates without EONS and in neonates with positive blood cultures compared with negative blood cultures.²³

The results of the ROC analysis for the IG Ratio, IG Percentage, and Absolute IG obtained the cut-off values for the IG Ratio of 2.21, IG Percentage (3.20), and IG Absolute (0.34). In the study, Hampson et al. reported that neutrophil function, IG count, and plasma cfDNA levels showed potential as biomarkers for the prediction or early diagnosis of sepsis and neutrophil dysfunction might actively contribute to the development of sepsis.²⁴ Meanwhile, the research conducted by Cimenti C et al., on patients with early-onset neonatal sepsis (EONS) and 112 controls showed IG results with a cut-off value of $0.24 \times 10^3/\mu\text{L}$.²³ According to the previous study, the diagnostic value will increase if the IG value is added with stab and blast cells. Differences in IG values can occur because the IG value itself is influenced by many things, including the administration of steroids to the mother during pregnancy, non-specific responses to physiological stresses associated with prematurity and many other pathological conditions such as cancer, trauma or myeloproliferative diseases that cause IG values increase.^{23,24}

In this study, a bivariate analysis of

risk factors for early-onset neonatal sepsis (EONS) was carried out with positive cultures for Immature Granulocyte (IG), namely IG Ratio, IG Percentage, and Absolute IG using the chi-squared test. The Odds Ratio (OR) Immature Granulocyte Ratio (IG Ratio) in this study was 8.021; thus, the group of patients with positive culture EONS with an IG Ratio of 2.21 had a risk factor of 8.021 times higher for the incidence of EONS. The study by Iddles C et al. explained that the threshold IG ratio of 0.35 had a sensitivity of 74% and a specificity of 35% for diagnosing sepsis.⁹ The study also reported that compared to CRP, the IG Ratio was more accurate in detecting sepsis.⁹ A similar study by Noviani I et al., also concluded that the IG ratio could be used as a predictor of infection and sepsis because the results of the calculation of the IG ratio are higher in patients with bacterial infections with positive blood culture results.¹⁰ Therefore, the IG ratio is a better predictor of infection than the leukocyte count.^{9,10}

Another study by Ansari-Lari MA et al., found a significantly higher IG percentage in infected patients than uninfected patients.²⁵ It concluded that an IG percentage of more than three (IG% > 3) could be used as a predictor of sepsis, with a specificity of more than 90%.²⁵ IG Absolute value has the highest positive predictive value of infection on days 3 to 5. It can be concluded that total IG can detect the presence of infection compared to CRP, LBP and IL-6, especially in the first 48 hours. Another problem is that the value of the cut-off point used by each hematology analyzer is different. A previous study reported a sensitivity of 74.4% for the IG Absolute and IG Percentage. However, other studies reported a specificity of 25.3% for IG Absolute and 26.6% for IG Percentage. In addition, the stability of the control sample worsens as the expiration date approaches.²⁵⁻²⁷

This study has a limitation, namely the Area Under Curve (AUC) parameter evaluation regarding Immature Granulocyte Ratio (IG Ratio) showing the lower limit of 95% CI of 0.490 and the upper limit of 95% CI of 0.851 so that it is statistically significant but clinically significant to be able to distinguish Sepsis. Early Onset Neonatorum (EONS) with

positive or negative cultures needs further evaluation.

CONCLUSION

The results of this study indicate that the cut-off point of Immature Granulocyte Ratio (IG Ratio) of 2.21 has a risk factor of 8.021 times higher, a sensitivity of 64.7%, and a specificity of 81.4% for diagnosing Early-Onset Neonatal Sepsis (EONS) in neonates with sepsis.

CONFLICT OF INTEREST

There is no competing interest regarding the manuscript.

ETHICAL APPROVAL

Ethics approval has been obtained from the Ethics Committee, Faculty of Medicine, Universitas Udayana, Prof. dr. I.G.N.G Ngoerah Hospital, Denpasar, with number 596/UN14.2.2VII.14/LT/2022 and LB.02.01/XIV.2.2.1/13393/2022.

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AUTHOR CONTRIBUTIONS

All authors equally contribute to this study from the conceptual framework, data acquisition, and data analysis until interpreting the study results through publication.

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