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The Relationship Between Red Cell Distribution Width (RDW) Value and Mortality Rate in Neonatorum Sepsis at Murni Teguh Methodist General Hospital Sussana Wesley

Muhammad Arief Pratama
Universitas Imelda Medan

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Email :
arief.inside@gmail.com

ABSTRACT

Neonatal sepsis remains the leading cause of morbidity and mortality in neonates. Accurate identification of prognostic factors is essential to improve management and clinical outcomes. This study aims to analyze the relationship between Red Cell Distribution Width (RDW) values and other clinical and laboratory parameters and mortality rates in neonatal sepsis. This cross-sectional study involved 98 neonates with a diagnosis of sepsis at Purely Teguh Methodist Sussana Wesley General Hospital from July to December 2023. Demographic, clinical, and laboratory data are collected and analyzed. The statistical tests used included chi-square, independent t-test, and Mann-Whitney U, with a $p<0.05$ value considered significant. Of the 98 neonates, 35 (35.71%) died. Septic shock was significantly more common in the group that died (85.71% vs 12.70%, $p<0.001$). Higher RDW values correlated with increased mortality (17.10% ± 1.72 vs 15.40% ± 1.28, $p<0.001$). Thrombocytopenia (173.00 ± 152.00 vs 242.50 ± 126.00 x 10^3/µl, $p=0.048$), increased IT ratio (median 0.42 vs 0.28, $p=0.018$), and higher procalcitonin levels (median 3.25 vs 0.68 ng/ml, $p=0.007$) were also associated with an increased risk of mortality. Septic shock, increased RDW values, thrombocytopenia, increased IT ratio, and high procalcitonin levels are significant predictors of mortality in neonatal sepsis. The combination of these parameters can improve accuracy in risk stratification and guide more effective clinical management.

INTRODUCTION

Neonatorum sepsis is one of the leading causes of morbidity and mortality in newborns worldwide. This condition is characterized by a systemic inflammatory response to infections that occur in the first 28 days of life. Although advances in neonatal care have improved survival rates, neonatal sepsis remains a major challenge in neonatal health care.

Early diagnosis and proper management are essential to improve the prognosis of neonatal sepsis. However, the clinical symptoms of sepsis in neonates are often non-specific, so reliable biomarkers are needed to aid in diagnosis and prediction of prognosis. One of the hematological parameters that has attracted attention in recent years is the Red Cell Distribution Width (RDW).

RDW is a measure of erythrocyte size variability that is routinely checked as part of a complete blood test. Although it was originally used to differentiate the type of anemia, recent research suggests that RDW has the potential to be a prognostic biomarker in a variety of conditions, including sepsis. Several studies have reported an association between increased RDW values and the severity and mortality of sepsis in the adult population. However, research on the role of RDW in neonatal sepsis is still limited.

Murni Teguh Methodist General Hospital Sussana Wesley, as one of the health care centers in Indonesia, has a neonatal care unit that handles cases of neonatal sepsis. Given the importance of identifying prognostic factors to improve the management of neonatal sepsis, this study aims to analyze the relationship between RDW values and mortality rates in neonatal sepsis in the hospital.

The results of this study are expected to provide new insights into the role of RDW as a prognostic biomarker in neonatal sepsis, as well as assist in risk stratification and clinical decision-making. In addition, this research can also be the basis for further studies on the use of RDW in the

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management of neonatal sepsis in Indonesia.

METHOD

Research Design This study uses a cross-sectional design to analyze the relationship between Red Cell Distribution Width (RDW) values and mortality rates in neonatal sepsis. Time and Place of Research The research was carried out at Murni Teguh Methodist Sussana Wesley General Hospital for a period of 6 months, from July 2023 to December 2023. Population and Sample The target population of this study is neonates who were diagnosed with neonatal sepsis and were treated in the neonatal care unit of Purely Teguh Methodist General Hospital Sussana Wesley. The research sample is 98 neonates who meet the inclusion and exclusion criteria.

Inclusion Criteria:

a. Neonates (age 0-28 days) who are diagnosed with neonatal sepsis based on clinical and laboratory criteria.
b. Have complete RDW examination data.

Exclusion Criteria:

a. Neonates with major congenital abnormalities.
b. Neonates who die within the first 24 hours of treatment.
c. Incomplete medical record data.

Sampling Technique Sampling is carried out by the consecutive sampling method, where all subjects who meet the inclusion and exclusion criteria during the research period are included in the study until the number of samples is met.

Research Variables

a. Independent variable: Red Cell Distribution Width (RDW) value
b. Dependent variable: Mortality in neonatal sepsis

Data Collection Data is collected from the patient's medical records, including:

a. Demographic characteristics (gestational age, birth weight, gender)
b. RDW value at the diagnosis of neonatal sepsis
c. Blood culture results (if available)
d. Clinical outcomes (alive or dead)

Data Analysis The data was analyzed using SPSS statistical software version 25.0. Univariate analysis was performed to describe the characteristics of the sample. The relationship between RDW values and mortality was analyzed using the chi-square test for categorical data and the independent t-test or Mann-Whitney U (depending on the data distribution) for numerical data. Multivariate analysis using logistic regression was performed to control potential confounding factors. The p value < 0.05 is considered statistically significant.

Research Ethics This research has been approved by the Health Research Ethics Committee of Murni Teguh Methodist General Hospital Sussana Wesley. The confidentiality of patient data is maintained by only using the medical record number as an identity.

RESULTS AND DISCUSSION

The study involved 98 neonates with a diagnosis of neonatal sepsis. The characteristics of the sample showed that the gender distribution was dominated by men as much as 57 (58.16%) compared to 41 (41.84%) for women.

The median gestational age of the sample was 38 weeks, with a range between 37 to 41 weeks, suggesting that most of the sample were full-term infants. The median age at diagnosis of sepsis is 2.5

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days, with a range of 0 to 29 days, indicating that most cases are diagnosed in the first week of life.

The birth weight of the sample had a median of 3000 grams, with a range from 2500 to 4500 grams, showing variations from normal weight to macrosomia. The majority of cases (85.71%) are Early Onset Neonatal Sepsis (SNAD), while 14.29% are Slow Onset Neonatal Sepsis (SNAL). Complications in the form of septic shock occurred in 38.78% of the samples. The mortality rate was quite high, with 35.71% of the sample experiencing a death outcome. The length of the hospital stay varies with a median of 10 days, ranging from 1 to 47 days.

Hematological parameters showed an average RDW of 15.70% (±1.68), hemoglobin 15.92 g/dL (±3.25), leukocytes 16.58 x 10^3/µl (±8.20), and platelets 220.50 x 10^3/µl (±140.20). The median value of the immature ratio to total neutrophils (IT ratio) is 0.37, with a wide range from 0.02 to 3.60. Procalcitonin levels, as a marker of inflammation, had a median of 1.06 ng/ml with a very wide range from 0.07 to 63.00 ng/ml, indicating variations in the severity of inflammation in the samples. Overall, these data describe a population of neonates with sepsis that have varied clinical and laboratory characteristics, with varying severity and outcomes.

Table 1. Characteristics of the study patients

Characteristic	(n=98)
Gender, n (%)	
- Men	57 (58,16)
- Woman	41 (41,84)
Gestational age, weeks; median (min-max)	38 (37-41)
Age, days; median (min-max)	2,5 (0-29)
Birth weight, grams; median (min-max)	3000 (2500-4500)
Onset sepsis, n (%)	
- SNAD	84 (85,71)
- SNAL	14 (14,29)
Syok septic, we (%)	38 (38,78)
Deceased Externals, n (%)	35 (35,71)
The duration of care, days; median (min-max)	10 (1-47)
RDW (%); rerata ±SD	15,70 ±1,68
Hemoglobin (g/dL); Average ±SD	15,92 ± 3,25
WBC (10^3/µl); rerata ±SD	16,58 ±8,20
Trombosit (10^3/µl); rerata ±SD	220,50 ±140,20
IT rasio; median (min-max)	0,37 (0,02-3,60)
Prokalsitonin (ng/ml); median (min-max)	1,06 (0,07-63,00)

Description: SNAD: Neonatal Sepsis Early Onset SNAL: Neonatal Sepsis Late-Onset

The study involved 98 neonates with sepsis, consisting of 63 surviving neonates and 35 dying. Analysis of the characteristics between these two groups shows some significant differences. The distribution of sex was relatively balanced between the two groups, with a slight dominance of males in both the surviving (57.14%) and dead (60.00%) groups. This difference was not statistically significant (p = 0.785).

Gestational age and birth weight did not show significant differences between the two groups. The median gestational age was 38 weeks for both groups (p = 0.652), while the median birth weight was slightly higher in the group that died (3050 grams vs 3000 grams, p = 0.558). The majority of cases in both groups were Early Onset Neonatal Sepsis (SNAD), with a higher proportion in the group who died (91.43% vs 82.54%), although this difference was not statistically significant (p = 0.375).

A very significant difference was seen in the incidence of septic shock. The group that died had a much higher proportion of septic shock than the group that survived (85.71% vs 12.70%, p < 0.001).

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Table 2. Comparison of the characteristics of living and deceased patients

Characteristic	Live (n=63)	Died (n=35)	P
Jenis kelamin, n (%)			
- Men	36 (57,14)	21 (60,00)	0,785
- Woman	27 (42,86)	14 (40,00)	
Gestational age, weeks; median (min-max)	38 (37-41)	38 (37-41)	0,652
Age, days; median (min-max)	3 (0-23)	2 (0-29)	0,890
Birth weight, grams; median (min-max)	3000 (2500-3900)	3050 (2520-4500)	0,558
Onset sepsis, n (%)			
- SNAD	52 (82,54)	32 (91,43)	0,375
- SNAL	11 (17,46)	3 (8,57)	
Syok septic, n (%)	8 (12,70)	30 (85,71)	<0,001
The duration of care, days; median (min-max)	10 (1-36)	9 (1-47)	0,460
RDW (%); rerata ±SD	15,40 ±1,28	17,10 ±1,72	<0,001
Hemoglobin (g/dL); Average ±SD	16,30 ±2,95	15,15 ±3,70	0,165
WBC (10^3/µl); Average ±SD	16,10 ±7,00	17,40 ±10,15	0,530
Trombosit (10^3/µl); Average ±SD	242,50 ±126,00	173,00 ±152,00	0,048
IT rasio; median (min-max)	0,28 (0,02-0,98)	0,42 (0,2-3,6)	0,018
Prokalsitonin (ng/ml); median (min-max)	0,68 (0,07-62,59)	3,25 (0,1-21,04)	0,007

Laboratory parameters show some important differences:

a. The RDW value was significantly higher in the group that died (17.10% ± 1.72 vs 15.40% ± 1.28, $p < 0.001$).
b. Platelet count was lower in the group that died (173.00 ± 152.00 x 10^3/µl vs 242.50 ± 126.00 x 10^3/µl, $p = 0.048$).
a. IT ratio was higher in the group that died (median 0.42 vs 0.28, $p = 0.018$).
b. Procalcitonin levels were also significantly higher in the group that died (median 3.25 ng/ml vs 0.68 ng/ml, $p = 0.007$).

There was no significant difference in terms of hemoglobin and leukocyte count between the two groups.

Length of stay did not show a significant difference between the two groups ($p = 0.460$). Overall, these results suggest that septic shock, higher RDW values, thrombocytopenia, increased IT ratio, and higher procalcitonin levels are closely related to an increased risk of mortality in neonates with sepsis. These findings may aid in the early identification of high-risk neonates and more intensive management to improve outcomes.

Discussion

This study analyzed the relationship between various clinical and laboratory parameters and mortality in neonatal sepsis. The results showed several factors that were significantly related to the increased risk of death in neonates with sepsis.

Red Cell Distribution Width (RDW): This study found that higher RDW values were associated with increased mortality in neonatal sepsis. These results are in line with a study by Martin et al. (2019) in the adult population with sepsis, which reported that an increase in RDW correlates with disease severity and mortality.

However, a study by Lee et al. (2021) in premature neonates did not find a significant association between RDW and sepsis mortality. This difference may be due to: a) Population variation: Our study included term and premature neonates, while Lee's study focused on premature neonates. b) Pathophysiological mechanisms: In term neonates, RDW may be more reflective of systemic inflammatory responses, whereas in premature, other factors such as hematopoietic system imagination may play a greater role.

Our findings on the association of thrombocytopenia with mortality of neonatal sepsis are consistent with the study of Ree et al. (2017), which reported that thrombocytopenia is an independent predictor of mortality in neonatal sepsis. However, a study by Ahmed et al. (2020) found that thrombocytopenia has a lower predictive value compared to other inflammatory markers such as C-reactive protein (CRP). This difference may be due to: a) Sampling time: Thrombocytopenia may develop more slowly compared to changes in acute inflammatory markers. b) Etiological variation: Different causes of sepsis (gram-positive vs negative bacteria) may affect the degree of thrombocytopenia differently.

The results of our study showing a higher IT ratio in the group with higher mortality correspond to the findings of Hornik et al. (2012), who reported that IT ratio is a strong predictor of early-onset sepsis. However, a study by Saboohi et al. (2019) found that the IT ratio has a lower sensitivity compared to procalcitonin in predicting neonatal sepsis. This difference may be due to: a) Variability in IT examination techniques and interpretation ratios between laboratories. b) The influence of non-infectious factors on the IT ratio, such as perinatal stress or antenatal steroid use.

Our findings on the prognostic value of procalcitonin are in line with a meta-analysis by Vouloumanou et al. (2015), which reported the high sensitivity and specificity of procalcitonin in the diagnosis of neonatal sepsis. However, some studies such as Chiesa et al. (2015) report variations in optimal procalcitonin cut-off values for the prediction of neonatal sepsis. This difference may be due to: a) Physiological variations in procalcitonin levels in neonates in the first few days of life. b) Differences in the etiology of sepsis and host immune responses in different populations and clinical settings.

The results of our study on the prognostic factors of neonatal sepsis show some similarities and differences with previous studies. This variation is interesting to analyze further to understand the complexity of neonatal sepsis and the challenges in predicting its output.

The difference in results we found with some other studies can be explained by several factors. First, the heterogeneity of the population studied plays an important role. Each neonatal care unit has unique patient characteristics, with variations in gestational age, birth weight, and comorbidities. For example, a unit that handles more extreme premature babies may face different challenges compared to a unit that handles more full-term babies. This can affect how various clinical and laboratory parameters correlate with outcomes.

Second, differences in operational definitions and management protocols between institutions can lead to variation in results. The definition of sepsis, septic shock criteria, or cut-off values for laboratory parameters may differ between studies. For example, some centers may use a stricter definition for septic shock, while others may use looser criteria. This can affect how patients are grouped and analyzed in the study.

Local factors also play an important role. Antibiotic resistance patterns, resource availability, and management protocols that differ between institutions can affect patient outcomes. A hospital with quick access to third-line antibiotics or advanced technology such as ECMO may have different outcomes compared to hospitals with limited resources.

Intervention timing is another crucial factor. The speed at which diagnosis and therapy is initiated can greatly affect the progression of the disease and the patient's outcomes. Hospitals with better early detection systems may be able to intervene earlier, influencing how prognostic parameters correlate with outcomes.

Furthermore, the complexity of the pathophysiology of neonatal sepsis cannot be ignored. Sepsis involves a complex interaction between pathogens, host immune responses, and environmental factors. Genetic variation, differences in immune system maturity, and maternal factors can affect how neonates respond to infection. This can lead to variability in how biomarkers such as RDW, platelets, or procalcitonin correlate with disease severity.

It is also important to consider that sepsis neonatorum is not a homogeneous disease entity. Differences in causative agents (gram-positive vs. negative bacteria, or even viral infections) can lead

to variations in clinical presentation and laboratory responses. Studies dominated by one type of pathogen may show different prognostic patterns compared to studies with a broader spectrum of pathogens.

Finally, methodological aspects such as sample size, study design, and statistical analysis techniques can also contribute to differences in outcomes between studies. Studies with larger sample sizes may be able to detect more subtle associations, while prospective studies may provide more robust data compared to retrospective studies.

Understanding these factors is important for interpreting the results of our research in a broader context. It also emphasizes the importance of a tailored approach in the management of neonatal sepsis, taking into account the specific characteristics of the population and specific clinical settings. In the future, multicenter studies with standardized protocols may be able to provide a more comprehensive understanding of the prognostic factors of neonatal sepsis, helping to develop more accurate and effective prediction and management strategies.

The results of this study emphasize the importance of close monitoring of signs of septic shock, as well as the use of a combination of biomarkers such as RDW, platelet count, IT ratio, and procalcitonin in assessing the risk of mortality in neonatal sepsis. This approach can help in risk stratification and more informed clinical decision-making.

The study had several limitations, including a cross-sectional design that did not allow for the assessment of causal relationships, as well as the possibility of unidentified confounding factors. Prospective studies with larger sample sizes are needed to confirm these findings.

CONCLUSION

The study identified several important prognostic factors in neonatal sepsis, with septic shock and increased RDW as strong predictors of mortality. This combination of clinical and laboratory parameters can improve accuracy in predicting outcomes and guide more effective management of neonatal sepsis.

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