

The Correlation between RDW, PDW, and NLR with the SOFA Score in Septic Patients

Linda Mayliana KN¹, Irda Handayani¹, Agus Alim Abdullah^{1,2}, Mansyur Arif^{1,2}

¹Department of Clinical Pathology, Faculty of Medicine, Hasanuddin University/Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia.
E-mail: lmayliana19@gmail.com

²Clinical Pathology Laboratory Labuang Baji Hospital, Makassar, Indonesia

ABSTRACT

Sepsis is one of the main causes of mortality in the intensive care unit. The SOFA score is used to assess organ dysfunction. There are several markers of sepsis such as the combination of RDW, PDW, and NLR to help predict the outcome of sepsis. To determine the role of RDW, PDW, and NLR associated with SOFA scores as prognostic markers in sepsis. A retrospective study with a cross-sectional approach has been conducted using secondary data from the medical records of sepsis patients from January 2018 to December 31, 2020, who met the inclusion criteria and were admitted to the ICU of Dr. Wahidin Sudirohusodo Hospital, Makassar. The sample size was 109 people consisting of 62 (56.9%) males and 47 (43.1%) females. The highest age range is 56–65 years (37.6%). A total of 97 people (89%) died and 12 (11%) improved. There is a positive correlation between changes in RDW and changes in SOFA scores ($p=0.031$), there is a positive correlation between changes in PDW and changes in SOFA scores ($p=0.000$), and there is a positive correlation between changes in NLR and changes in SOFA scores ($p=0.000$). The increase of RDW caused by systemic inflammation can predict disease progression. The state of increased proinflammatory cytokines inhibits the proliferation and maturation of erythrocytes; hence, it causes an increase in RDW. The acceleration of platelet destruction due to the suppression of cytokines in the bone marrow increases PDW. The increase in NLR occurs due to the rise in the inflammatory response, which results in suppressed cellular immunity. RDW, PDW, and NLR are positively correlated with changes in SOFA scores. PDW and NLR have a significant correlation with the outcome. RDW, PDW, and NLR can be used as prognostic markers in septic patients.

Keywords: Sepsis, RDW, PDW, NLR, SOFA score

INTRODUCTION

Sepsis is a life-threatening condition with organ dysfunction where there is a dysregulation of the body's response toward infection. Organ failure is one of the reasons for high mortality and morbidity in the Intensive Care Unit (ICU), so an assessment model was developed to describe the severity of the diseases in patients treated in the ICU, namely Sequential Organ Failure Assessment (SOFA). Clinically, it can be explained that organ dysfunction happens when there is an increase of 2 or more in the SOFA score.^{1,2}

There were 494 cases of sepsis at Dr. Wahidin Sudirohusodo Hospital in 2020. Mortality of septic patients in the ICU is still high, data that was obtained from the ICU of Dr. Wahidin Sudirohusodo Hospital in 2020 showed 139 cases, 88% mortality cases, and 12% recoveries.

The SOFA Score is used as an assessment of sepsis that is calculated based on clinical and laboratory parameters. Six organ systems (lungs,

cardiovascular, kidneys, central nervous system, and coagulation) were assessed on a score from 1 to 4. The number of laboratory parameters in the SOFA score assessment will cause an increase in the hospital bills of the patients in the ICU. There are also other parameters to estimate the prognosis of a septic or septic shock patient. These parameters must be able to reflect the inflammation concept that plays a role in sepsis pathophysiology. The parameters in the Complete Blood Count (CBC) examination that can be used to predict sepsis are Red cell Distribution Width (RDW), Platelet Distribution Width (PDW), and Neutrophile Lymphocyte Ratio (NLR). Ni *et al.* proposed the use of NLR on admission as a mortality predictor due to sepsis in the hospital. Sari *et al.* showed that NLR is a biomarker that is available to plenty and rapid in differentiating septic patients. Neutrophil lymphocyte ratio has been recommended as a bacteremia predictor that is better than routine parameters such as C-Reactive Protein (CRP), leukocyte count, and neutrophile count.³⁻⁵

New studies have been linked as a prognostic factor in several critical conditions, including sepsis. Khrisna et al. found that an increase in RDW 72 hours after receiving care can predict mortality. Zang *et al.* reported that the combination of RDW, PDW, and NLR showed a high diagnostic performance to predict sepsis. RDW, PDW, and NLR are all routine examinations and are relatively cheap compared to other examinations. Based on this, this study analyses the values of RDW, PDW, and NLR as prognostic markers in septic patients in the Intensive Care Unit (ICU) at Dr. Wahidin Sudirohusodo Hospital, Makassar.^{1,6}

METHODS

This was a retrospective cross-sectional study using secondary data from the medical records of patients of Dr. Wahidin Sudirohusodo Hospital, from January 2018 until December 2020. The population of this study were patients that were treated in the ICU of Dr. Wahidin Sudirohusodo Hospital that was diagnosed with sepsis and met the inclusion criteria of age over 18 years old and below 65 years old, had RDW, PDW, and NLR examinations on day 1 and 3 of ICU treatment. Vital signs, GCS, thrombocyte, total bilirubin, creatinine, and blood gas analysis for SOFA score on days 1 and 3 were conducted. Patients diagnosed with ITP, DHF, and pregnancy were excluded. RDW, PDW, and NLR examinations were conducted on the Sysmex automatic cell counter analyzer.

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Statistical data analysis was calculated and processed using SPSS software.

RESULTS AND DISCUSSIONS

This research showed that from 109 samples, there were 62 (56.9%) males and 47 (43.1%) females with an age range of 18-65 years old, and the most common age range is 56-65 years old, as much as 41 (37.6%) patients. Ninety-seven (89%) patients passed away, while 12 (11%) patients recovered (Table 1).

Table 1. Study subjects characteristics

Criteria	n (%)
Gender	
Male	62 (56.9%)
Female	47 (43.1%)
Age	
18-35 years old	23(21.1%)
36-45 years old	18(16.5%)
46-55 years old	27(24.8%)
56-65 years old	41(37.6%)
Outcome	
Recovered	12(11%)
Died	97(89%)

Source: Secondary data

Table 2 shows the distribution of RDW, PDW, NLR, and SOFA score days 1 and 3 of the study population. RDW day 1 between 11.3–30.3 with a mean of 15.7 ± 3.0 . PDW day 1 between 8.0–28.2 with a mean of 12.6 ± 3.5 . NLR day 1 between 2.9–67.8 with a mean of 16.6 ± 11.8 . SOFA score day 1 between 4–13 with a mean of 6.6 ± 1.9 . RDW day 3 between 12.2–30.3 with a mean of 16.6 ± 2.8 . PDW day 3 between 8.1–31.2 with a mean of 14.3 ± 4.0 . NLR day 3 between 3.1–85.1 with a mean of 20.1 ± 14.1 . SOFA score day 3 between 3–19 with a mean of 7.4 ± 2.6 .

Table 2. Descriptive distribution of RDW, PDW, NLR, and SOFA scores on day 1 and day 3 of the study population

Variable	Minimum	Maximum	Mean	SD	p
Day 1					
RDW	11.3	30.3	15.7	3.0	<0.001
PDW	8.0	28.2	12.6	3.5	<0.001
NLR	2.9	67.8	16.6	11.8	<0.001
SOFA score	4	13	6.6	1.9	<0.001
Day 3					
RDW	12.2	30.3	16.6	2.8	<0.001
PDW	8.1	31.2	14.3	4.0	<0.001
NLR	3.1	85.1	20.1	14.1	<0.001
SOFA score	3	19	7.4	2.6	<0.001

Kolmogorov-Smirnov test

Table 3. Correlation analysis of RDW, PDW, and NLR with the SOFA score on day 1 and day 3

Variable	SOFA Score	
	R	p
Day 1		
RDW	0.002	0.983
PDW	0.106	0.275
NLR	0.939	0.000
Day 3		
RDW	0.075	0.441
PDW	0.160	0.097
NLR	0.876	0.000

*Statistical tests using Spearman's correlation test; R: correlation coefficient, $p < 0.05$

Table 3 does not show a correlation between day 1 RDW and PDW with SOFA score day 1. There was a significant positive correlation between day 1 NLR and SOFA score day 1 ($p=0.000$). There was no correlation between day 3 RDW and PDW with SOFA

score day 3. There was a significant positive correlation between day 3 NLR and SOFA score day 3 ($p=0.000$).

Table 4. Correlation analysis of changes in RDW, PDW, and NLR with changes in SOFA score

Variable	SOFA Score Changes	
	R	p
Changes RDW	0.206	0.031
PDW	0.364	0.000
NLR	0.695	0.000

*Statistical test using Spearman's correlation test. R: correlation coefficient, $p < 0.05$

Table 4 shows a significant positive correlation between the changes in RDW, PDW, and NLR with changes in the SOFA score ($p < 0.05$).

Figure 1 shows a positive correlation with the increase of RDW, PDW, and NLR are proportional to the increase in SOFA score.

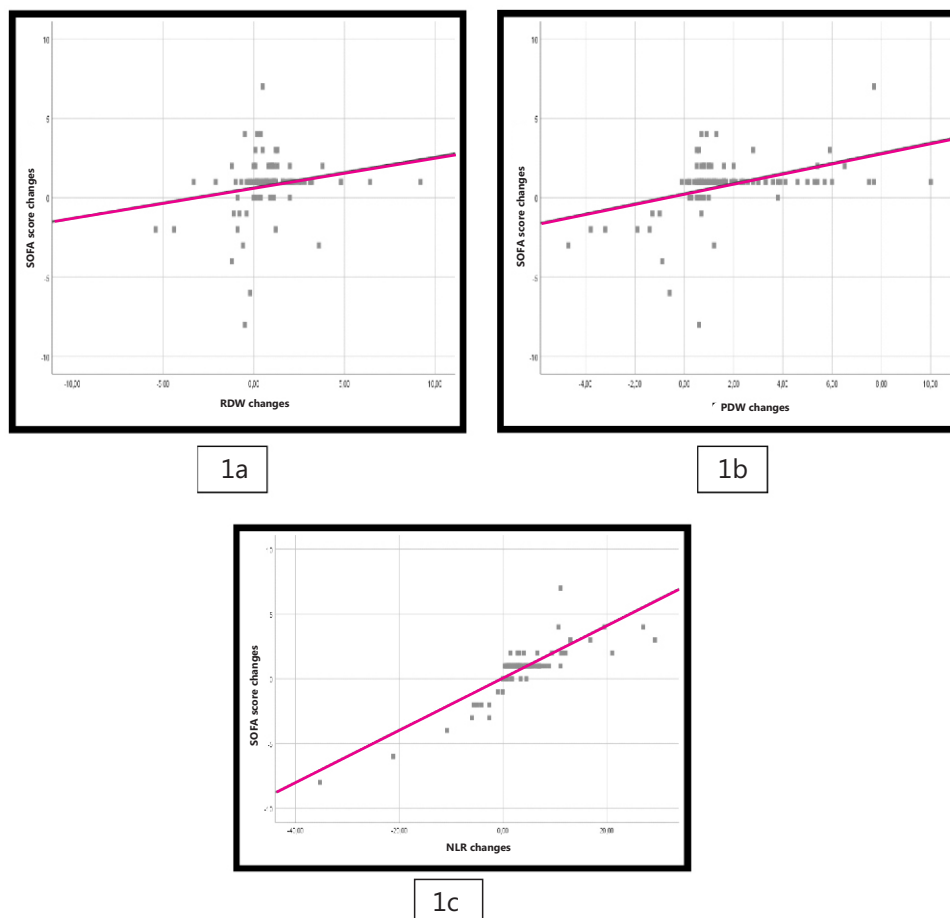


Fig 1 (a). The correlation of RDW changes with SOFA score changes; (b) the correlation of PDW changes with SOFA score changes; (c) the correlation of NLR changes with SOFA score changes

Table 5. Relationship between RDW, PDW, and NLR day 1 and day 3 with the outcome of the patient

Variable	Day 1 Mean		p	Day 3 Mean		p
	Recovered	Died		Recovered	Died	
RDW	17.1	15.5	0.257	16.2	16.6	0.419
PDW	12.2	12.7	0.934	10.8	14.8	<0.001
NLR	15.6	16.7	0.058	7.7	21.7	<0.001

Statistical testing using Mann-Whitney, significant if $p < 0.05$

Table 5 shows that there was no significant relationship between RDW, PDW, and NLR on day 1 with the outcome of the patients. There was no relationship between day 3 RDW with the outcome, while there was a significant relationship between PDW and NLR day 3 with the patient's outcome ($p < 0.001$).

This study was conducted in August 2021 by obtaining secondary data from inpatients that were diagnosed with sepsis from January 1st, 2018 until 31 December 2020 at Dr. Wahidin Sudirohusodo Hospital. There was a total of 109 data obtained from patients treated in the ICU. There were more male patients (56.9%) compared to female patients (43.1%). This study also found that septic patients that died during treatment in the ICU were higher than those that recovered (89%). The age range most prone to sepsis was 56–65 years old (37.6%). A study by Puneekar *et al.* showed that male patients were more prone to sepsis compared to female patients. Based on the data above, male patients suffered from sepsis more than females, probably because they are more active outside the home, so they are more often exposed to pathogenic bacteria; another possibility is that the production of immunoglobulin and genetic or humoral antibodies are lower in males than in females. Several risk factors play a role in sepsis such as age, gender, race, comorbidities, genetics, corticosteroid therapy, chemotherapy, and obesity. Inflammation response is better in younger ages than older ones.⁷

This study showed that RDW significantly increased with the increase of SOFA score ($r=0.206$, $p=0.031$), these results are in line with the study by Mohammed *et al.*, SOFA score > 10 has RDW $> 15.2\%$ with $p < 0.001$. They concluded that septic patients with high SOFA scores also had longer duration in the ICU and higher RDW. Another study by Krisna *et al.* found that RDW changes in the first 72 hours after hospital admittance have a significant impact on all causes of mortality, and they found that an increase of RDW in the first 72 hours is a dynamic risk

marker in septic patients and as a predictor of mortality. These findings are in line with this study.^{1,8}

Red cell distribution width increase that is caused by systemic inflammation can predict disease progressivity. Proinflammatory cytokines obstruct erythrocyte proliferation and maturation that is induced by erythropoietin, which causes structural and functional changes in the red blood cell. Septic conditions and an increase in proinflammatory cytokines can cause an increased RDW.¹

In this study, PDW had a significant positive correlation, while an increase in PDW was proportional to an increase in SOFA score ($r=0.364$, $p=0.000$), this is in line with research conducted by Zang *et al.* where an increase in PDW indicates bacterial sepsis. In sepsis, compensation occurs caused by accelerated platelet destruction due to direct interaction with proinflammatory cytokines and suppression of bone marrow cytokines, causing an increased PDW in septic patients.⁶

This study found a significant positive correlation between changes in NLR and changes in SOFA scores ($r=0.695$, $p=0.000$), where an increase in NLR was proportional to an increase in SOFA score. This study is in line with Zang *et al.* where there was a significant correlation between an increase in NLR and an increase in SOFA score in bacterial sepsis with $p < 0.001$. Neutrophils play an important role in the innate immune response that results in organ failure and even death, whereas lymphocytes play an important role in the adaptive immune response indicating inflammation. Huang *et al.* stated that neutrophils are the first leukocytes to migrate from the blood to the site of infection to kill pathogens and remove cellular debris. At the beginning of infection, neutrophils tend to decrease, but as the infection progresses, the number of neutrophils tends to increase both in terms of number and distribution. At the same time, lymphocyte apoptosis in the thymus gland and spleen increases, resulting in a decrease in lymphocytes. The increase in NLR occurs due to an increase in the inflammatory

response which results in suppressed cellular immune responses.^{5,9}

The limitations of this study were that many medical records did not record the patients' SOFA scores so the author calculated the score using available data. This could differ from the actual condition of the patient and there were a lot of data that we excluded due to the incomplete parameters needed to calculate the SOFA score, causing the number of samples to be reduced

CONCLUSIONS AND SUGGESTIONS

A significant positive correlation for NLR was only in the first and third days. The changes in PDW and NLR had positive correlations with SOFA scores. Platelet distribution width and NLR correlate with the results.

Further research is needed with more samples to obtain better research results and as a prognostic indicator of patients with sepsis.

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