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Neutrophil-Lymphocyte Ratio as a Mortality Predictor in Intensive Care Patients

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ABSTRACT
Systemic inflammatory response markers such as lactate, C-reactive protein, and procalcitonin are commonly used to predict mortality in intensive care unit patients. One potential alternative to these markers is the neutrophil-lymphocyte ratio, which can be calculated based on a patient's blood cell count. This study aims to determine the potential of the neutrophil-lymphocyte ratio as a predictor of length of stay and mortality in intensive care patients. This study employed an analytical cross-sectional design, conducted at the Intensive Care Unit of Royal Prima Hospital in Medan, involving 170 patients. The data used in this study were secondary data obtained from patients' medical records. The results of this study found that the majority of intensive care patients had a neutrophil-lymphocyte ratio greater than 3 (94.1%), were hospitalized for less than 7 days (84.7%), and 92.4% of patients died during their hospitalization. Data analysis revealed that although the neutrophil-lymphocyte ratio was not significantly associated with the length of stay ($p > 0.05$), patient mortality was significantly associated with both the neutrophil-lymphocyte ratio ($p < 0.005$) and the length of stay ($p < 0.05$). Multivariate analysis revealed that patient mortality in the intensive care unit was influenced by the neutrophil-lymphocyte ratio and length of hospitalization, with the neutrophil-lymphocyte ratio being the most significant factor affecting patient mortality ($p < 0.005$; OR: 11.978). It can be concluded that the neutrophil-lymphocyte ratio is a reliable predictor of mortality in intensive care patients, but its accuracy in predicting patient length of stay is less pronounced.

Keywords: *ength of stay, mortality, NLR, intensive care*

INTRODUCTION
Intensive care patients generally have higher morbidity and mortality compared to other wards in a hospital. Intensive care patients require specialised care management to improve their outcomes and optimise their quality of life. Patients are admitted to the intensive care unit (ICU) because of infection, heavy bleeding, burn injury, neurovascular incidents, cardiovascular incidents, sepsis, or post-surgery, which all lead to massive inflammation (Mamo et al., 2023; Sakr et al., 2018; Unal et al., 2015; Wang et al., 2025).

Intensive care patients' length of stay and mortality are determined by the underlying conditions and their severity, medications, and immunological response disorders, along with the number of procedures the patient had undergone, such as intubation, mechanical ventilation, and vascular access (Ababneh et al., 2022; Kalın et al., 2022). The Acute Physiology and Chronic Health Evaluation II score (APACHE II) is commonly used to assess patients' mortality risks within the first 24 hours after admission to the ICU (Hardisman, 2008; Qu et al., 2020). Other inflammatory markers, such as C-reactive protein and procalcitonin, are also commonly used to assess patients' mortality; however, the tests

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for these inflammatory markers are not readily available and are relatively more expensive (Ismy, 2015; Qu et al., 2020).

The neutrophil-lymphocyte ratio is an affordable marker that can be calculated using readily available complete blood count results by dividing the absolute neutrophil count by the absolute lymphocyte count (Martins et al., 2019). NLRs represent the balance between neutrophils, a crucial component of innate immunity and the inflammatory response, and lymphocytes, which are central to adaptive immunity; hence, NLRs describe the homeostasis of the immune system (Buonacera et al., 2022; Zhang et al., 2021). Since its first publication by Roman Zahorec in 2001, NLR has been widely studied to assess inflammation in patients and to evaluate the risks of mortality among critically ill patients (Zahorec, 2001, 2021; Zahorec et al., 2020).

METHODS

This study aims to assess the relationship and the effect of NLR on the length of stay and mortality of intensive care patients. This study employs an analytic observational design with a cross-sectional approach. This study was conducted in the Intensive Care Unit of Royal Prima Hospital, Medan, Indonesia, in December 2024. The population of this study is all intensive care patients between June 2023 and June 2024, and the sample was selected using stratified random sampling, with a sample size of 170. Data for this study were obtained from the medical records of patients in the intensive care unit. The data in this study were analysed using binary logistic regression analysis. This study was declared ethically fit by the Health Research Ethics Committee of Universitas Prima Indonesia (Letter No. 021/KEPK/UNPRI/v/2024).

RESULTS

Among the 170 patients' data used for this study, the majority were male (54.7%), were senior (74.1%), and had one comorbidity (52.9%). The majority of patients also have an NLR greater than three (94.1%), stay less than 7 days in the ICU (84.7%), and did not survive (92.4%).

Table 1 Patient Characteristics, NLR, Length of Stay, and Mortality

Characteristics	n	%
Sex		
Male	93	54.7
Female	77	45.3
Age group		
Adult	44	25.9
Senior	126	74.1
Comorbidities		
Without Comorbidities	41	24.1
One Comorbidities	90	52.9
Two Comorbidities	36	21.2
Three Comorbidities	3	1.8
NLR		
≤3	10	5.9
>3	160	94.1
Length of Stay		
≤ 7 days	144	84.7
> 7 days	26	15.3
Mortality		
Survive	13	7.6
Dead	157	92.4
Total	170	100.0

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A chi-square test was conducted to ascertain the relationship between patients' characteristics and their length of stay. However, no significant relationship was found between sex, age group, comorbidities, and NLR and patients' length of stay in the intensive care unit (p-value > 0.05) (Table 2).

Table 2. Relationship Between Cofactors and NLR with Length of Stay

	Length of Stay						p-value
	≤7 Days		>7 Days		Total		
	n	%	n	%	n	%	
Sex							
Male	82	56.9	11	42.3	93	54.7	0.168
Female	62	43.1	15	57.7	77	45.3	
Age group							
Adult	40	27.8	4	15.4	44	25.9	0.184
Senior	104	72.2	22	84.6	126	74.1	
Comorbidities							
Without Comorbidities	34	23.6	7	26.9	41	24.1	
One Comorbidities	80	55.6	10	38.5	90	52.9	0.334
Two Comorbidities	28	19.4	8	30.8	36	21.2	
Three Comorbidities	2	1.4	1	3.8	3	1.8	
NLR							
≤3	8	5.6	2	7.7	10	5.9	0.670
>3	136	94.4	24	92.3	160	94.1	

Although no significant relationship was found between patients' characteristics and their length of stay in the intensive care unit, a significant relationship was found between the NLR and patients' mortality (p-value < 0.001) and between the length of stay and patients' mortality (p-value < 0.05) (Table 3).

Table 3. Relationship Between Cofactors, NLR and Length of Stay with Mortality

	Mortality						p-value
	Survive		Dead		Total		
	n	%	n	n	%	n	
Sex							
Male	4	30.8	89	56.7	93	54.7	0.071
Female	9	69.2	68	43.3	77	45.3	
Age group							
Adult	5	38.5	39	24.8	44	25.9	0.281
Senior	8	61.5	118	75.2	126	74.1	
Comorbidities							
Without Comorbidities	6	46.2	35	22.3	41	24.1	
One Comorbidities	6	46.2	84	53.5	90	52.9	0.220
Two Comorbidities	1	7.7	35	22.3	36	21.2	
Three Comorbidities	0	0.0	3	1.9	3	1.8	
NLR							
≤3	4	30.8	6	3.8	10	5.9	0.000
>3	9	69.2	151	96.2	160	94.1	
Length of Stay							
≤ 7 days	8	61.5	136	86.6	144	84.7	0.016
> 7 days	5	38.5	21	13.4	26	15.3	

A multivariate analysis was also conducted using a binary logistic regression test. It was found that NLR and length of stay were significant predictors of mortality in intensive care

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patients, with NLR being the stronger predictor (p-value < 0.005; OR: 10.819). Although comorbidities were found not to be a significant predictor of mortality, the relatively higher OR compared to the length of stay cannot be overlooked. By using the β value from Step II, the probability of intensive care patients dying when patients have an NLR greater than three and length of stay longer than seven days is 71.3% if patients have no comorbidity, 93.0% if patients have one comorbidity, 98.6% if patients have two comorbidities, and 99.7% if patients have three comorbidities.

Table 4 The Effect of NLR, Length of Stay, and Other Cofactors on Mortality

	β	*p-value*	OR	CI 95%	
				Lower	Upper
Step I					
Sex	-0.982	0.151	0.375	0.098	1.430
Comorbidities	0.876	0.061	2.401	0.961	5.996
NLR	2.213	0.007	9.147	1.818	46.012
Length of stay	-1.483	0.033	0.227	0.058	0.884
Constant	1.009	0.628	2.743		
Step II					
Comorbidities	0.808	0.081	2.244	0.905	5.564
NLR	2.381	0.004	10.819	2.181	53.677
Length of stay	-1.511	0.029	0.221	0.057	0.858
Constant	-0.764	0.648	0.466		

DISCUSSION

In this study, an analysis of 170 intensive care patients, comprising 93 male patients and 77 female patients, revealed a significant association between NLR and length of stay in predicting patient mortality. The majority of patients in this study had NLR values greater than three (94.1%), thus exceeding the threshold established by Zahorec (Zahorec, 2021). The mortality rate among patients in this study was very high, with only 7.6% of ICU patients surviving their stay at the ICU. Additionally, 15.9% of patients in this study were hospitalized for more than seven days.

The high mortality rate in the ICU is uncommon when compared to ICU mortality rates in previous studies. A meta-analysis of sepsis cases found that the mortality rate of sepsis patients admitted to the ICU was only 41.9% (Fleischmann-Struzek et al., 2020). This high mortality rate suggests that the population studied in this study had severe and critical conditions and were in an advanced stage of the disease or had experienced multiple organ failure.

This study found a significant association between increased NLR values and mortality (*p-value*<0.005), with NLR serving as a robust predictor of mortality (*p-value*<0.005), where the odds ratio of patient death with increased NLR reached 10.111; ICU patients with an NLR >3 had a 10.111 times higher risk of death compared to ICU patients with an NLR ≤3. This finding is supported by previous studies that have investigated the prognostic function of NLR in the context of intensive care. A study on COVID-19 patients admitted to the ICU found that NLR was significantly correlated with patient mortality outcomes, with deceased patients having an average NLR of 11.3 ± 10.93, while survivors had an NLR of 5.8 ± 7.45 (Seyfi et al., 2023). Another study in 2022 also found that NLR can predict COVID-19 patient mortality with high specificity and sensitivity (>70%) (Regolo et al., 2022). Additionally, in critically ill patients or those with severe injuries who did not survive (died), NLR values were significantly higher compared to survivors, suggesting that NLR can serve as an independent predictor of patient mortality (Djordjevic et al., 2018). In the study by Doganay and Cirik (2022), significant differences were found between COPD patients

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admitted to the ICU who survived and those who did not, with surviving patients having an average NLR value of 16.43 ± 30.00, while the average NLR value for non-surviving patients reached 25.94 ± 30.96 (Doganay & Cirik, 2022). In this study, no significant association was found between NLR and patient length of stay (*p-value* > 0.05).

These results are inconsistent with previous studies that found NLR to be significantly associated with length of stay and a good predictor of length of stay (El-Menyar et al., 2024; Mirna et al., 2021; Olivo et al., 2023; Santos et al., 2024). In Olivo et al.'s (2023) study on patients with epilepsy, it was found that NLR not only predicts patient length of stay (*p-value* < 0.05; β = 0.759) but also predicts the risk of ICU admission (p-value < 0.05; OR = 1.065) (Olivo et al., 2023). However, in patients post-surgery due to gastrointestinal perforation, it was found that length of stay was associated with NLR, and that length of stay could only be predicted by the patient's preoperative absolute leukocyte count (Al-Yahri et al., 2021). A systematic review of eight studies on NLR, length of stay, and mortality found that NLR has adequate predictive ability for hospital stay duration in patients, and an increase in NLR is positively correlated with length of stay (Qiu et al., 2022).

Although NLR was not found to be associated with length of stay in this study, length of stay was found to be associated with patient mortality (p-value < 0.05). Furthermore, in multivariate analysis, it was found that NLR and length of stay together influence patient mortality. This complex relationship suggests that while a longer length of stay is associated with mortality outcomes, NLR remains a better and more accurate predictor of mortality. The significant association between length of stay and mortality indicates that patients who remain longer in ICU care have a higher risk of complications or exhibit more severe patient conditions, thereby requiring longer care duration. This association is supported by previous studies, which have found that the overall length of hospital stay (not just in the ICU) is associated with and significantly influences mortality in COPD patients (Doganay & Cirik, 2022). However, other studies did not find a significant association between ICU length of stay and patient mortality (Zhao et al., 2024). The differences in results among these studies may be due to differences in patient length of stay categorization, where in this study, patient length of stay was categorized using a seven-day *cut-off* value, while in the two previous studies, the patient length of stay *cut-off* was 30 days and continuous (Djordjevic et al., 2018; Zhao et al., 2024).

In one of the most extensive registry studies (n: 448,574), it was found that NLR can predict the risk of hospitalization (hazard ratio/HR: 1.18) and premature death (HR: 1.45) significantly (Liu et al., 2024). Although NLR does not have better predictive value for premature mortality than CRP, NLR still has better predictive value for patient mortality than CBC (Liu et al., 2024). Additionally, a systematic review of 79,943 COVID-19 patients found that elevated NLR levels were significantly associated with disease severity, increased risk of intensive care unit admission, and mortality (Abdullah et al., 2024). These findings suggest that NLR is a prognostic tool that can be used in the care of critically ill patients, though it should be used in conjunction with other markers and/or comprehensive risk assessments. Research has even found that, in the context of COVID-19, although NLR has similar specificity to CRP as an inflammatory marker, NLR exhibits higher sensitivity than CRP (NLR: 72.9%; CRP: 60.2%) (Regolo et al., 2022).

In addition to the effects of NLR and length of stay on mortality, this study also aimed to investigate the impact of sex, age, and the number of comorbidities on patient mortality in intensive care patients. In this study, sex was not found to influence ICU patient mortality (*p-value* > 0.05). Several studies have found that the influence of sex on ICU patient mortality cannot be observed as a single factor but rather as a result of interactions between various factors such as age, diagnosis, and other conditions. In a study of cardiac arrest patients in Switzerland, it was found that although women had higher ICU mortality, the likelihood of women being admitted to the ICU due to cardiac arrest was lower than that of men (Amacher et al., 2025). Meanwhile, a meta-analysis of 229 studies with a total of 10 million patients found that males generally have a higher risk of being admitted to the ICU

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and have higher mortality rates (Pijls et al., 2022). In addition to sex, age was not found to influence patient mortality in this study. These findings contradict previous studies that have found patient age, particularly among seniors, to increase the risk of mortality significantly (de Lange et al., 2024; Jackson et al., 2021; Mesas et al., 2020; Nachtigall et al., 2021). The study by Nachtigall et al. (2021), which involved over 23,000 patients diagnosed with COVID-19 in Germany, found that patient age significantly impacts COVID-19 mortality, both in patients admitted to the ICU and those not admitted to the ICU. The study found that in non-ICU patients, the risk of mortality increased after the age of 50, while in ICU patients, the risk of mortality increased after the age of 40 and increased sharply after the age of 65 (Nachtigall et al., 2021). One possible reason for this difference in results is the abnormal distribution of age data in this study, as indicated by the high number of patients aged 50 years or older.

The only confounding factor identified as affecting ICU patient mortality in this study was the number of comorbidities. In this study, it was found that an increase in the number of comorbidities increased the probability of mortality in ICU patients, although the effect was not statistically significant. This finding is supported by previous studies that found that comorbidities in ICU patients influence ICU patient mortality, and multimorbidity significantly increases the risk of patient mortality (Cardoso et al., 2020; Simpson et al., 2020; Vallet et al., 2021). The study by Vallet et al. (2021), a systematic review of 129 studies in Europe and North America involving patients aged 75 years or older, found that patient comorbidities can predict mortality in the ICU. During the COVID-19 pandemic, ICU patients requiring mechanical ventilation and having one or more comorbidities had a higher mortality risk compared to patients without comorbidities (Cardoso et al., 2020; Simpson et al., 2020). The presence of comorbidities in ICU patients, one or more, imposes a higher physiological burden on the body. Additionally, multimorbidity/comorbidities lead to continuous inflammation, which increases oxidative stress on organs and tissues, causing cellular mitochondrial dysfunction (Bezerra et al., 2023; Cifuentes et al., 2024).

CONCLUSION

It can be concluded that NLR is a valuable and accurate predictor of mortality among intensive care patients. Since it utilises the already available complete blood count, using NLR to assess the mortality risk in intensive care patients will not incur any additional cost. However, its predictive ability needs to be compared with other traditional markers, such as CRP or procalcitonin.

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