Prognostic Value of the Neutrophil–Lymphocyte Ratio for 28-Day Mortality in Hospitalized Pulmonary Tuberculosis

Ali Napiah Nasution[1], Perwita Sari Sinaga[2], Sri Wahyuni Nasution[3]

[1]Master's Program in Tropical Medicine, Faculty of Medicine, Dentistry and Health Sciences, Universitas Prima Indonesia, PUI PHYTO Degenerative and Lifestyle Medicine, Universitas Prima Indonesia
[2]Master's Program in Tropical Medicine, Faculty of Medicine, Dentistry and Health Sciences, Universitas Prima Indonesia
[3]Master's Program in Tropical Medicine, Faculty of Medicine, Dentistry and Health Sciences, Universitas Prima Indonesia, PUI PHYTO Degenerative and Lifestyle Medicine, Universitas Prima Indonesia

Email correspondence: alinapiahnasution@unprimdn.ac.id

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Abstract

Pulmonary tuberculosis (TB) remains a leading cause of infectious mortality. The neutrophil–lymphocyte ratio (NLR) is an accessible inflammatory index that may stratify short-term risk in hospitalized TB. To examine whether admission NLR predicts 28-day mortality in pulmonary TB. We conducted a retrospective cohort at Royal Prima General Hospital, Medan (1 January 2023–31 December 2024), among adults (18–65 years) admitted with active pulmonary TB. Demographics, TB category, day-1 neutrophil and lymphocyte counts (to derive NLR), and 28-day outcomes were abstracted from medical records. NLR was analyzed as a continuous variable and as a binary variable using a receiver operating characteristic (ROC)-derived cut-off. Group comparisons used t/Mann–Whitney tests as appropriate; prognostic performance was assessed by area under the ROC curve (AUC). The results of the analysis show that NLR has a significant ability to identify patients at risk of death during treatment. This finding has important implications for clinical management, where the use of NLR as a routine biological marker can assist medical personnel in triage and more timely therapeutic decision-making. Therefore, the application of this parameter is expected to help reduce mortality rates through closer monitoring of high-risk patient groups.

Keywords: Pulmonary Tuberculosis, Neutrophil–Lymphocyte Ratio, 28-Day Mortality, Prognosis, Biomarkers.

INTRODUCTION

Pulmonary TB infection remains a serious health problem, especially in developing countries with limited health systems and facilities (Ong et al., 2020). According to data from the World Health Organization (WHO), there were 10.7 million cases of tuberculosis (TB) in 2023, increasing to 10.8 million cases worldwide with an incidence of 134 cases per 100,000 population and a mortality rate of 1.25 million. These figures make TB the leading cause of death from a single infection worldwide (World Health Organization, 2024). Indonesia ranks second in the world for the highest number of TB cases, with an estimated 354 cases per 100,000 population in 2021 (Badan Kebijakan Pembangunan Kesehatan, 2023). In 2024, North Sumatra ranked third among provinces with the highest number of TB cases in Indonesia, after

West Java and East Java, with 74,434 cases, or 7.1% of the total TB cases in Indonesia. The highest number of cases was recorded in Medan, with 3,775 cases (Kemenkes RI, 2023).

The use of NLR as a clinical tool has become routine in medical care and treatment for various medical conditions. A study by Rajalingam et al. (2022) found that NLR is a more sensitive marker of bacterial infection than leukocyte count for diagnosing acute appendicitis. Kilci et al. (2025) noted that NLR is a more effective predictor of bacteremia than C-Reactive Protein (CRP) levels, white blood cell count, and single neutrophil count in the emergency department (ED). Additionally, NLR's ability to predict patient survival rates across various clinical conditions at a relatively affordable cost and with widespread availability supports its application in medical decision-making and planning across healthcare facilities (Hong et al., 2022).

The clinical value of NLR is based on the pathophysiological mechanisms and development of pulmonary TB, in which an increase in neutrophil count occurs due to activation of phagocytosis to eliminate Mtb (Rahman, 2024). A decrease in lymphocyte count occurs due to a left shift in leukocyte distribution, neutrophilia, and lymphocyte accumulation at the focus of pulmonary infection (Kabak et al., 2020). The NLR value generally increases within 6 hours of the onset of infection and physiological stress, reflecting acute inflammatory conditions more accurately than other complete blood count components that take longer to change (Kosidło et al., 2023).

Gu et al. (2023) stated that high NLR values are associated with an increased risk of 28-day mortality in TB patients and are positively correlated with the severity of TB infection. This demonstrates the clinical significance of NLR in evaluating the prognosis and severity of TB infection in the short term (Chai et al., 2023). The study by Sheng et al. shows that NLR values are significantly associated with pulmonary TB mortality in hospitals (OR 0.42; $p = 0.04$). Additionally, NLR can also distinguish and identify pulmonary TB patients with a high mortality risk (AUC 79%; $p < 0.001$) (Sheng et al., 2025).

Royal Prima General Hospital (RSU) Medan is a type B private hospital that routinely treats pulmonary TB patients and can perform complete blood tests independently. The NLR biomarker has also been routinely used to assist in the care and treatment of pulmonary TB patients at this health facility. However, there is no data showing the significance and relationship of NLR to the mortality rate of pulmonary TB patients treated at RSU Royal Prima Medan. Therefore, this study aims to determine the effect of the Neutrophil-Lymphocyte Ratio (NLR) parameter on the mortality of pulmonary TB patients treated at Royal Prima General Hospital in Medan in 2023–2024.

METHODS

We conducted a retrospective cohort study to evaluate the relationship between the neutrophil-lymphocyte ratio (NLR) at hospital admission and 28-day mortality among adult patients admitted to the inpatient ward of Royal Prima General Hospital, Medan, with a diagnosis of pulmonary tuberculosis (TB). Eligible participants were all patients aged 18–65 years with a diagnosis of active pulmonary TB who were treated between January 1, 2023, and December 31, 2024. This study involved 286 samples of pulmonary TB patients treated at Royal Prima General Hospital, Medan, during the period 2023–2024. Research samples were selected using the total sampling method, in which the entire population that met the inclusion and exclusion criteria was included as a sample in this study. The inclusion criteria included patients aged 18–65 years, patients diagnosed with active pulmonary TB, pulmonary TB patients treated in the inpatient ward of Royal Prima General Hospital, Medan, during the period January 1, 2023–December 31, 2024, and patients who underwent a complete blood test upon admission to Royal Prima General Hospital, Medan. Exclusion criteria included patients who were pregnant or breastfeeding; patients with extrapulmonary TB; patients with weakened immune systems (autoimmune diseases, AIDS, cancer, history of chemotherapy, history of organ transplantation) and/or currently receiving immunosuppressive therapy; patients with hematological disorders unrelated to pulmonary TB; patients with incomplete medical records; patients who did not undergo a complete blood count showing neutrophil and lymphocyte counts at the start of hospitalization; and TB diagnoses made after > 48 hours of hospitalization. Ethical approval was obtained from the Health Research Ethics Committee of Prima Indonesia University, with institutional permission from the hospital; all identities were kept confidential.

Statistical analysis was performed using SPSS v26 (IBM, Windows). Data normality was evaluated using the Kolmogorov–Smirnov test. Descriptive statistics were presented as the mean (standard deviation) for normally distributed variables or the median (minimum–maximum) for others. NLR was analyzed both as a continuous variable and as a categorical variable based on the optimal cutoff obtained from receiver operating characteristic (ROC) curve analysis. Continuous NLR group comparisons between survivors and non-survivors used binary regression tests or Mann–Whitney tests for non-normal data. The prognostic performance of NLR for 28-day mortality was evaluated using the area under the ROC curve (AUC); sensitivity, specificity, and predictive values were calculated at the selected cutoff value. A two-sided p-value < 0.05 was considered statistically significant.

RESULTS

Table 1. Characteristics of Neutrophil, Lymphocyte, and NLR Levels

Characteristics	Neutrophil Level	Lymphocyte Level	NLR Level
Gender			
Man	75.09 ± 11.52	15.58 ± 8.35	6.32 ± 3.83
Women	72.3 ± 13.05	16.91 ± 7.96	5.47 ± 3.52
Types of Pulmonary TB			
New TB Cases	72.32 ± 13.28	17.52 ± 8.93	5.41 ± 3.61
TB Relapses	75.78 ± 9.17	14.68 ± 6.7	6.41 ± 3.49
Drug-Resistant TB	0	0	0
TB Treatment Interruptions	78.56 ± 11.06	12.54 ± 6.65	7.91 ± 4.21
28-Day Outcome			
Survival	73.59 ± 12.12	16.42 ± 8.28	5.79 ± 3.62
Death	79.53 ± 10.59	12.3 ± 6.82	8.23 ± 4.22

Sex-stratified summaries showed higher inflammation indices in males than in females: males had mean (SD) neutrophils of 75.09 (11.52), lymphocytes of 15.58 (8.35), and NLR of 6.32 (3.83), whereas females had 72.30 (13.05), 16.91 (7.96), and 5.47 (3.52), respectively. By TB category, the loss-to-follow-up group exhibited the highest NLR (7.91 [4.21]) alongside higher neutrophils (78.56 [11.06]) and lower lymphocytes (12.54 [6.65]); the relapse group showed intermediate values (neutrophils 75.78 [9.17], lymphocytes 14.68 [6.70], NLR 6.41 [3.49]); and new cases had the lowest NLR (5.41 [3.61]) with neutrophils 72.32 (13.28) and lymphocytes 17.52 (8.93). Outcome-stratified data indicated that non-survivors within 28 days had higher neutrophil counts and lower lymphocyte counts—yielding a higher NLR—than survivors (neutrophils 79.53 [10.59], lymphocytes 12.30 [6.82], NLR 8.23 [4.22] vs 73.59 [12.12], 16.42 [8.28], 5.79 [3.62], respectively). Collectively, these patterns are consistent with greater systemic inflammatory burden among non-survivors and in clinically more complex TB categories.

Table 2. Analysis of the Relationship between NLR Values and Pulmonary TB Mortality

Outputs	Level NLR	*p-value**	OR (95% CI)
Survival	5.79 ± 3.62	<0.001	1.134 (1.045 – 1.231)
Death	8.23 ± 4.22		

A comparative analysis of the mean NLR values between the two disease outcome groups was performed using the Mann-Whitney test. The mean NLR values in the survival and death groups were 5.79 ± 3.62 and 8.23 ± 4.22, respectively, with a statistically significant difference ($p < 0.001$). The mean difference between groups of 2.44 confirms that NLR values tend to be higher in pulmonary TB patients who died within 28 days of admission to the hospital. The results of the binary regression analysis showed a significant effect of NLR on short-term pulmonary TB mortality, with a 1-point increase in NLR associated with a 13.4%

increase in mortality risk. The significance of these results is indicated by a 95% confidence interval (CI) range of 1.045–1.231.

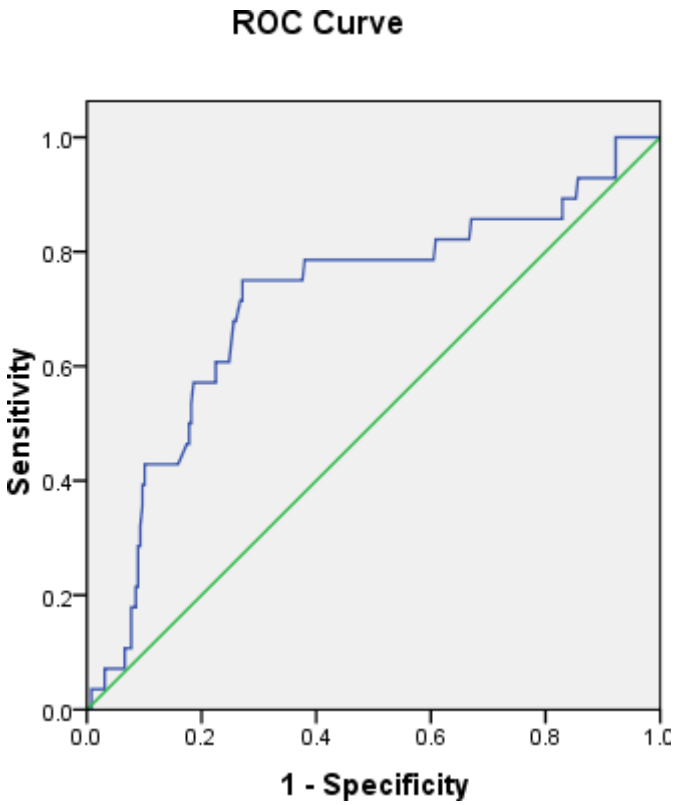

Figure 1. Analysis of NLR Value Prediction as a Predictor of Pulmonary TB Mortality

Receiver Operating Characteristics (ROC) curve analysis was performed to evaluate the ability of NLR values to predict 28-day mortality in patients with pulmonary TB treated in hospitals. The results of the ROC curve analysis showed that NLR values had an area under the curve (AUC) of 0.712 with a standard error (SE) of 0.056, a 95% confidence interval (95% CI) ranging from 0.602 to 0.822, and $p < 0.001$.

An AUC value of 0.712 indicates that NLR values are quite effective in identifying pulmonary TB patients at high risk of death within 28 days of admission to hospital, with higher NLR values associated with an increased risk of 28-day mortality in TB patients. The relatively narrow 95% confidence interval indicates that this parameter has good discriminatory accuracy. The p-value < 0.001 indicates a highly significant effect and relationship between NLR values and 28-day mortality in hospitalized TB patients.

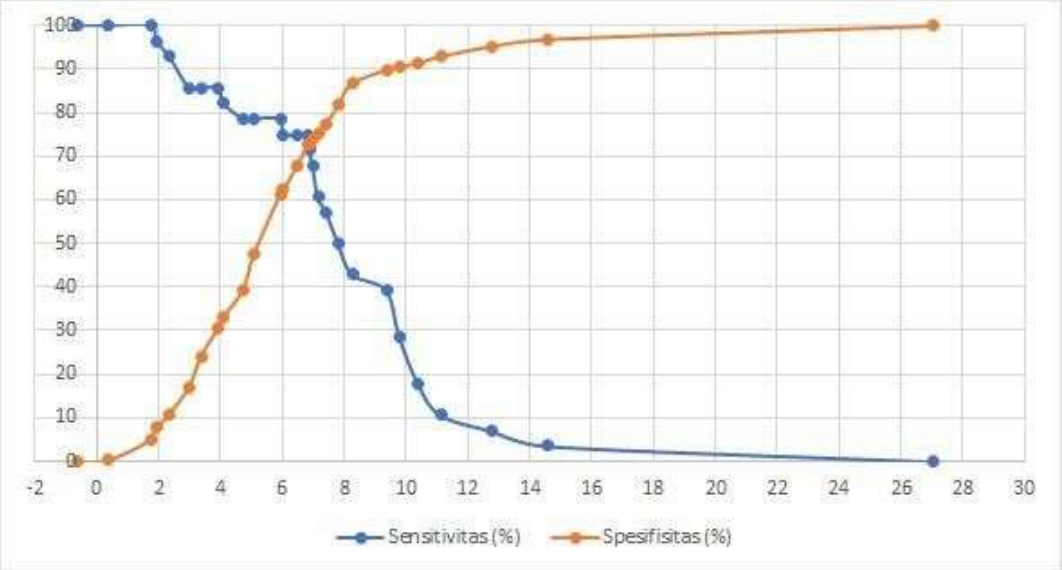

Figure 2. The best NLR threshold value for 28-day mortality in hospitalized TB patients

Based on the figure above, the best NLR cutoff value for predicting 28-day mortality in hospitalized TB patients is 6.845. The graph also shows that this value has the best sensitivity and specificity among other cutoff values, namely 75% and 72.9%. The positive predictive value (PPV), negative predictive value (NPV), and accuracy of the cutoff value can be analyzed based on the TyG values of the samples and the incidence of KKvM found in this study.

Table 3. Analysis of TyG Values in Samples to Predict KKvM Events

NLR	28-Day Outcome		Sensitivity	Specificity	NPV	PPV	Accuracy
	Life	Death					
< 6.845	188	7	75%	72.9%	96.4%	23.1%	73.1%
≥ 6.845	70	21					

An NLR cut-off value ≥ 6.845 has a sensitivity of 75% and specificity of 72.9% in predicting 28-day mortality in hospitalized pulmonary TB patients. This indicates that NLR has a fairly good ability to identify pulmonary TB patients at high risk of mortality within 28 days and to identify patients who survive. An NPV value of 96.4% indicates that almost all pulmonary TB patients with an NLR < 6.845 have a higher probability of surviving at the end of the 28-day period. This indicates the potential of NLR in stratifying the risk of survival in hospitalized pulmonary TB patients. Overall, the accuracy of NLR at this cutoff reached 73.1%, reflecting fairly good short-term prognostic performance in hospitalized pulmonary TB cases.

However, the PPV value of 23.1% is considered low. This figure reflects that an NLR ≥ 6.845 carries a high mortality risk, but only a small proportion of the population actually died within 28 days of hospitalization. This confirms that NLR is more appropriately used as a risk stratification tool, particularly to identify patients with a high likelihood of a good prognosis, rather than as a sole predictor of mortality.

DISCUSSION

The Effect of NLR on Pulmonary TB Mortality in Hospitals

The results of this study prove that the neutrophil-lymphocyte ratio (NLR) is a significant prognostic indicator of short-term clinical outcomes in patients with pulmonary tuberculosis (TB). These findings show that high levels of systemic inflammation, reflected in the predominance of neutrophils over lymphocytes, are strongly correlated with the risk of death within the critical 28-day period. Specifically, each increase in NLR value indicates an increase in patient vulnerability to fatal outcomes, suggesting that NLR may serve as a highly sensitive early warning biomarker.

The results of this study are consistent with those of Stanciu et al. (2025), which show that NLR is a systemic inflammatory marker associated with treatment duration and prognosis in pulmonary TB cases. An increase in NLR reflects a combination of reactive neutrophilia due to granulopoiesis stimulation by proinflammatory cytokines and relative lymphopenia triggered by lymphocyte redistribution and apoptosis, as well as other adaptive immune response dysfunctions (Minici et al., 2023). This condition is found in severe TB patients and is associated with an increased risk of early mortality. Gu et al. (2023) noted that NLR is an independent predictor of 28-day mortality in TB patients (OR ≈ 1.07 per unit of NLR) and that patients with high NLR tend to have a worse prognosis within 28 days.

Elevated NLR values in TB patients who die in the short term reflect more severe systemic inflammation and failure of the adaptive immune response (Ji et al., 2025). This is consistent with clinical findings where patients with poor prognoses tend to have higher NLR values upon hospital admission (Regolo et al., 2022). This is consistent with the findings of Suryana et al. (2022), who concluded that pre-treatment NLR values are associated with poor prognosis and delayed sputum conversion in pulmonary TB (Suryana et al., 2022). This empirical data supports the interpretation that NLR is not merely a passive inflammatory marker but rather an indicator of disease activity and greater mycobacterial load in the group at risk of death within 28 days.

An increase in the number of neutrophils in the severe phase of the disease contributes directly to tissue damage and organ dysfunction through the release of proteases, reactive oxygen species (ROS), and the formation of neutrophil extracellular traps (NETs), while a decrease in the number of lymphocytes indicates a disruption in the adaptive immune system, which is essential for controlling Mtb bacteria (Liu & Wang, 2021). Gu found that high NLR values were associated with increased 28-day mortality and clinical severity in TB patients.

These results support the role of NLR as a short-term prognostic marker in severe TB cases (Gu et al., 2023).

The Ability of NLR to Predict Pulmonary TB Mortality

This study shows that the neutrophil-lymphocyte ratio (NLR) threshold value has significant practical value as an initial screening tool for predicting short-term mortality in hospitalized patients with pulmonary tuberculosis. The discriminatory ability of this biomarker is moderate but effective in separating patients at risk of fatality from those who have a high chance of survival during the critical four-week period. The main advantage of this parameter lies in its very high negative predictive value, which provides clinical certainty that patients with hematological profiles below this threshold are almost certain to survive, allowing the medical team to focus on standard management.

Although its sensitivity is high enough to screen out most at-risk patients, its low positive predictive value indicates that a high inflammatory profile does not automatically mean death but should be interpreted as an early warning signal requiring intensive monitoring. These findings are consistent with the global literature, which positions NLR not as a definitive determinant but as an efficient and accessible risk stratification biomarker to direct medical attention to the most vulnerable groups. Therefore, integrating NLR monitoring into routine protocols can help clinicians triage pulmonary TB patients more accurately.

PPV and NPV values are not only influenced by sensitivity and specificity from an epidemiological perspective (Jiang et al., 2020). The prevalence rate in the tested population significantly impacts these values, where at relatively low mortality prevalence, PPV tends to decrease while NPV remains high (Ben-haim et al., 2024). Therefore, NLR is more relevant as an initial risk stratification tool (rule out high risk if NLR is low or flag for further evaluation if high) and should be used in combination with other clinical parameters or biomarkers, such as albumin levels, C-reactive protein (CRP), radiological findings, and history of comorbidities, before making aggressive therapeutic decisions (Özkan, 2024).

From a clinical perspective, NLR has strong clinical utility because it is readily obtained from a complete blood count and can stratify risk at the triage stage (Galardo et al., 2025). The potential of NLR is not limited to its diagnostic role but also as a parameter for therapeutic evaluation and prognosis (Yang et al., 2020). A decrease in NLR values in patients responding to therapy also demonstrates the usefulness of NLR for monitoring treatment response and identifying patients requiring more aggressive intervention (Kucukkarapinar et al., 2024). However, the interpretation of NLR must consider other factors, such as malnutrition, comorbidities, or the use of immunosuppressive drugs, which can affect neutrophil and

lymphocyte counts. Therefore, NLR should be used in conjunction with other clinical markers and severity scores for clinical decision-making (Arianmanesh et al., 2025).

Although this study provides strong evidence regarding the prognostic value of the Neutrophil-Lymphocyte Ratio (NLR), there are several limitations that need to be considered, such as the retrospective cohort design that relies on medical record data and the limited scope of the study to a single center, which limits the generalization of the findings. One important point is the relatively low positive predictive value (PPV) of 27.3%. Statistically, this low PPV is due to the low prevalence of mortality (28-day mortality) in this cohort population, because PPV is highly dependent on the prevalence of events in the field; even if the test has high sensitivity, the probability of someone actually dying among those with a high NLR remains low. However, this is offset by a very high negative predictive value (NPV) of 97.6%, indicating that NLR is more effective as a 'screening' tool for identifying low-risk and stable patients. The clinical implication of these findings is that NLR can be used as an economical initial triage tool to prioritize intensive monitoring of patients with NLR values above the threshold, thereby optimizing the management of medical resources in hospitals.

CONCLUSIONS

This study concludes that the neutrophil-lymphocyte ratio (NLR) is a reliable independent predictor of short-term mortality risk in hospitalized patients with pulmonary tuberculosis. A high NLR level upon hospital admission reflects the intensity of systemic inflammation, which is directly associated with poor patient prognosis. As a practical measure, the use of this parameter is highly recommended for medical personnel to quickly and affordably classify patient risk. For future researchers, it is recommended to conduct a prospective multicenter study with a larger sample size to validate a universal NLR threshold. Additionally, the integration of NLR with other clinical scoring systems or additional inflammatory biomarkers needs to be explored to improve the accuracy of mortality prediction in patients with pulmonary tuberculosis.

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