



Research Article

Correlation between Neutrophil-to-Lymphocyte Ratio and Severity of Community-Acquired Pneumonia in Patients

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ABSTRACT

The high morbidity and mortality rates due to pneumonia in developing countries indicate that a more affordable marker is needed to determine the degree of inflammation in cases of pneumonia infection. The neutrophil-to-lymphocyte ratio (NLR) is a simple indicator used extensively in evaluating the systemic inflammatory response. An observational cross-sectional study of 297 pneumonia patients was conducted using medical records as the source document. The patients' blood was taken during the hospital admission to obtain neutrophil and lymphocyte values. Meanwhile, the PSI score was used during the hospital admission to assess the severity of the pneumonia. Bivariate analysis using Spearman correlation was used to determine the correlation between NLR and pneumonia severity. The ROC curve was used to determine the cut-off value of NLR to distinguish mild from severe patients. The results of the Spearman correlation test analysis showed that the correlation between the NLR and the pneumonia severity was significantly positive ($r = 0.130$; $p = 0.025$). Furthermore, the median NLR value was higher in patients with severe pneumonia than in those with milder pneumonia severity (13.01 vs. 11.79 vs. 6.75). The NLR cut-off value of 9.07 was obtained to differentiate patients with mild severity and those with more severe disease. In conclusion, there is a correlation between the neutrophil-to-lymphocyte ratio and the severity of patients' pneumonia.



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INTRODUCTION

Pneumonia is also one of the leading reasons for hospitalization of adults worldwide, but the case fatality ratio of adult pneumonia in developing countries is much higher compared to the industrialized world (Aston, 2017). Community-acquired pneumonia prevalence worldwide estimates between 1.5 and 14 per 1000 individuals per annum, depending upon geography, time of year, and population (Regunath & Oba, 2022). However, pneumonia is more common in developing countries, like Indonesia. Based on the RISKESDAS 2018, pneumonia prevalence was around 2%, 1.8% in 2013. In 2010, pneumonia was one of the top 10 inpatient diagnoses in Indonesian hospitals, with a crude fatality rate (CFR) of 7.6% (Perhimpunan Dokter Paru Indonesia, 2020).

The higher morbidity and mortality due to pneumonia in developing countries imply that the inflation level in pneumonia infection has to be set at an economic marker. Neutrophil-lymphocyte ratio (NLR) is a simple marker commonly used in the diagnosis of systemic inflammatory response (Guthrie et al., 2013). The rise in NLR arises from neutrophilia and lymphopenia, an indicator of generalized inflammatory response (Pantzaris et al., 2018).

NLR is commonly utilized as a marker for diagnosis and mortality risk of community-acquired pneumonia (Zahorec, 2021). As of now, though, no research indicates the correlation between NLR and the severity of pneumonia, as well as the cut-off value between mild pneumonia and severe pneumonia. Identifying the cut-off value of NLR for the detection of each severity of pneumonia can help decide the treatment of pneumonia patients. Clinicians may use it to manage patients on an outpatient basis or admit them as inpatients. This data may give clinicians

more information about patients' inflammation status, leading to better management, which ultimately reduces hospital mortality.

METHODS

This cross-sectional study involved pneumonia subjects hospitalized in the pulmonary ward of RSUD Dr. Soetomo, Surabaya, between January 2019 and December 2019. The data were obtained from the medical records of RSUD Dr. Soetomo Medical Records Center and the Communication and Information Technology Installation. Inclusion criteria comprise subjects aged ≥ 18 years old with pneumonia hospitalized in RSUD Dr. Soetomo pulmonary ward. Subjects with incomplete or unclear medical records were excluded. The diagnosis of pneumonia was obtained from history taking, clinical manifestation, physical examination, chest x-ray, and laboratory examination (Musher & Thorner, 2014).

Clinical characteristics of pneumonia were divided according to the severity of the disease based on the Pneumonia Severity Index (PSI) scoring during hospital admission. PSI consists of 20 variables, namely demography, comorbid, and clinical variables, dividing pneumonia patients into five risk classes (Fine et al., 1997). Pneumonia patients were divided into several categories of risk classes, namely mild (PSI 1–2), moderately severe (PSI 3–4), and severe (PSI 5) (Aujesky et al., 2005). NLR value was obtained from the calculations of absolute neutrophil count divided by absolute lymphocyte count (Forget et al., 2017). NLR was also obtained during hospital admission. This study was approved by the Ethical Committee of Dr. Soetomo General/Teaching Hospital Surabaya (0902/LOE/301.4.2/V/2022).

Statistical analysis was performed using SPSS version 25.0 software (IBM Corporation, Armonk, NY, USA). A normality test was



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conducted for continuous data. Bivariate analysis was performed by Spearman correlation to determine the correlation between two variables. A p-value of < 0.05 was considered significant. ROC curve analysis was used to determine the cut-off value of NLR to differentiate between mild and severe pneumonia. This research is approved by the ethical Committee of Dr. Soetomo General/Teaching Hospital Surabaya (0902/LOE/301.4.2/V/2022).

RESULTS

Out of 514 potential subjects, 297 were eligible for this study's enrollment. The characteristics of subjects based on the PSI scoring category are shown in Table 1. The mean age of the subjects was 59.22 years old, with most males (62.4%). Among eligible subjects, 38 (12.8%) had mild pneumonia, 199 (67.0%) had moderately-severe pneumonia, and 60 (20.2%) had severe pneumonia. None of the subjects (0%) were nursing home residents. The subjects mostly had comorbidities (68.4%), with the neoplastic disease found in most subjects (59.9%). Pleural effusion on radiographic imaging was also found in most subjects (59.0%).

The characteristics of the subjects were then grouped by considering the pneumonia severity according to PSI score (Table 2). The mean age of the subjects in the more severe pneumonia was older than in the milder pneumonia group, with the severe pneumonia group having older patients with a mean age of 66.13 ± 12.33 years, the moderately severe having geriatric patients with a mean age of 59.97 ± 12.66 years, and mild pneumonia group having younger patients compared to the two more severe pneumonia, with the mean age of 44.37 ± 13.07 years. Unlike the mild group, moderately-severe and severe pneumonia were dominated by male subjects.

Only two listed comorbidities were found in subjects with mild pneumonia: neoplastic disease (26.3%) and heart failure (5.3%). More comorbidities were found in subjects with the moderately-severe and severe pneumonia, with the most frequent comorbidities being a neoplastic disease in both groups. However, subjects in the severe pneumonia group were more likely to have multiple comorbidities (23.3%) compared to the moderately-severe pneumonia group (6.5%). Abnormal findings in physical and laboratory examinations were rarely found in subjects with mild pneumonia. Pleural effusion was also more frequently detected in subjects with moderately-severe pneumonia (61.8%) and severe pneumonia (66.7%) than in those with mild pneumonia (28.9%).

Spearman correlation test revealed a significant positive correlation between NLR and pneumonia severity ($r=0.130$; $p<0.05$). The severe pneumonia group had a higher NLR value than the moderately-severe and mild pneumonia groups (13.01 vs 11.79 vs 6.75), albeit nonsignificant. However, the severity of the disease was significantly correlated with death incidence (Spearman correlation test: $r=0.238$; $p<0.001$), meaning that more severe groups had a higher risk of death. The cut-off value of NLR was obtained to predict pneumonia severity, which would help predict mortality. A cut value of NLR was 9.070, which meant that an NLR higher than the obtained result could mean more severe pneumonia. However, this cut-off neither has high sensitivity nor specificity.



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Table 1. The characteristics of subjects with pneumonia

Characteristics	Value (n = 297)
Pneumonia severity	
Mild	38 (12.8%)
Moderately-Severe	199 (67.0%)
Severe	60 (20.2%)
Sex, n (%)	
Male	186 (62.4%)
Female	111 (37.4%)
Age (years old), mean \pm SD	59.22 \pm 14.07
Nursing home resident, n (%)	0 (0%)
Comorbid, n (%)	
Neoplastic disease	178 (59.9%)
Heart failure	31 (10.4%)
Cerebrovascular disease	17 (5.7%)
Kidney disease	7 (2.4%)
Liver disease	2 (0.7%)
Physical Examination, n (%)	
Altered mental status	47 (15.8%)
RR \geq 30 breaths/min	49 (16.5%)
Pulse \geq 125 beats/min	36 (12.1%)
Sistole <90 mmHg	11 (3.7%)
Temperature >39.9°C or <35°C	0
Laboratory findings based on PSI category, n (%)	
pH <7.35	83 (27.9 %)
PaO ₂ <60 mmHg	25 (8.4%)
Glucose \geq 14 mmol/dL	23 (7.7%)
Sodium <130 mmol/L	41 (13.8%)
BUN \geq 11 mmol/dL	91 (30.6%)
HCT <30%	72 (24.2%)
Pleural effusion, n (%)	174 (59.0%)
Complete blood count findings, median (min-max)	
Leukocyte (x 10 ⁹ /L)	13.37 (1.12 – 113.88)
Neutrophil (x 10 ⁹ /L)	11.08 (0.89 – 82.30)
Lymphocyte (x 10 ⁹ /L)	0.94 (0.07 – 6.23)
NLR, median (min-max)	11.89 (1.01 – 120.50)
Death, n (%)	146 (49.2%)

**Table 2.** The characteristics of the subject are based on the severity of the disease

Characteristics	Mild Pneumonia (n=38)	Moderately-Severe Pneumonia (n=199)	Severe Pneumonia (n = 60)
Sex			
Male	18 (47.4%)	125 (62.8%)	43 (71.7%)
Female	20 (52.6%)	44 (22.1%)	17 (28.3%)
Age (years old), mean±SD	44.37±13.07	59.97±12.66	66.13±12.33
Nursing home resident	0 (0%)	0 (0%)	0 (0%)
Comorbid			
Neoplastic disease	10 (26.3%)	125 (62.8%)	43 (71.7%)
Heart failure	2 (5.3%)	20 (10.1%)	9 (15.0%)
Cerebrovascular disease	0 (0%)	9 (4.5%)	8 (13.3%)
Kidney disease	0 (0%)	3 (1.5%)	4 (6.7%)
Liver disease	0 (0%)	1 (0.5%)	1 (1.7%)
Physical Examination			
Altered mental status	0 (0%)	23 (11.6%)	24 (40.0%)
RR ≥30 breaths/min	0 (0%)	30 (15.1%)	19 (31.7%)
Pulse ≥125 beats/min	2 (5.3%)	23 (11.6%)	10 (16.7%)
Sistole <90 mmHg	0 (0%)	2 (1.0%)	7 (11.7%)
Temperature >39.9°C or <35°C	0 (0%)	0 (0%)	0 (0%)
Laboratory findings based on PSI category, n (%)			
pH <7.35	2 (5.3%)	46 (23.1%)	35 (58.3%)
PaO2 <60 mmHg	0 (0%)	12 (6.0%)	13 (21.7%)
Glucose ≥14 mmol/dL	1 (2.6%)	17 (8.5%)	5 (8.3%)
Sodium <130 mmol/L	1 (2.6%)	59 (29.6%)	25 (41.7%)
BUN ≥11 mmol/dL	9 (23.7%)	15 (7.5%)	23 (38.3%)
HCT <30%	8 (21.1%)	44 (22.1%)	20 (33.3%)



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Pleural effusion, n (%)	11 (28.9%)	123 (61.8%)	40 (66.7%)
Complete blood count findings, median (min-max)			
Leukocyte	11.90 (2.33 – 38.24)	13.99 (1.12 – 13.43)	(5.37 –
Neutrophil	9.93 (1.52 – 35.36)	113.88)	35.49)
Lymphocyte	1.24 (0.20 – 3.14)	11.46 (0.89 – 40.96)	11.42 (3.72 –
		0.93 (0.10 – 6.23)	31.79)
			0.89 (0.07 – 2.76)
NLR, median (min-max)	6.75 (1.64 – 42.62)	11.79 (1.01 – 13.01)	(2.01 –
		113.78)	120.50)
Deaths, n (%)	13 (34.2%)	99 (49.7%)	34 (56.7%)

Table 3. NLR cut-off point to differentiate between milder to more severe pneumonia

Characteristic	NLR
<i>Cut-off</i>	9.07
Sensitivity	0.637
Specificity	0.579
Area	0.631
CI 95%	0.528 – 0.733
<i>p-value</i>	0.009

DISCUSSION

Infectious diseases lead to elevated circulating white blood cells, including pneumonia. Changes in the number and components of leukocytes in the form of neutrophilia and lymphocytopenia are physiological reactions of the natural immune system against inflammation in bacterial infections (Gibot & Cravoisy, 2020). Our study found that pneumonia patients tend to experience leukocytosis, absolute neutrophilia, and absolute lymphocytopenia. The tendency of pneumonia patients to experience both neutrophilia and lymphocytopenia meant that pneumonia patients had a higher risk of elevated NLR. NLR, as the ratio obtained from absolute neutrophil count divided by absolute lymphocyte count, shows the balance between two immune system aspects; acute and chronic inflammations are evaluated through the neutrophil count, while adaptive immunity is represented by the lymphocyte

count (Angkananard et al., 2018). NLR discloses a better equilibrium of neutrophils and lymphocytes than absolute leukocyte count (Chen et al., 2017).

Our study found that the median NLR of pneumonia patients was 11.89, which was significantly higher than the NLR value in healthy, non-geriatric adults (Forget et al., 2017). This finding corresponded with the literature declaring that NLR for pneumonia patients is considerably higher compared to healthy adults (Cataudella et al., 2017). However, elevated NLR in this study may also be influenced by the elderly subjects. Li et al., in their research, disclosed that NLR is higher in the elderly compared to the young in a healthy population (<20 years) (Li et al., 2015).

NLR level was also elevated along with the severity of the disease, although the difference was not significant. Mujakovic et al. and Peng et al. declared that higher pneumonia severity is also followed by a higher NLR median



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(Mujakovic et al., 2020; Peng et al., 2021). A study by Huang et al. also disclosed that NLR increases along with PSI score (Huang et al., 2022).

The neoplastic disease may be associated with higher NLR findings in pneumonia patients since neutrophilia is correlated with it (Grivennikov et al., 2010). Other than neoplastic diseases, systemic autoimmune disease and their treatments might increase the risk of infection and lower the lymphocyte count (Takahashi et al., 2020). Higher NLR findings in moderately-severe and severe pneumonia may also be linked to histories of heart diseases, stroke, and chronic kidney disease frequently found in both groups. The diminished immunological function is attributable to the above-mentioned conditions, which result in the inability to fight off pathogens (Kalil et al., 2021). The body's inability to fend off harmful pathogens leads to a worse prognosis, eventually leading to death.

In this study, there is a significantly higher proportion of moderately-severe pneumonia patients compared to the other groups. This is in adherence to admitting moderately severe pneumonia patients to regular hospital wards while admitting mild pneumonia patients as outpatients and severe pneumonia patients to the ICU. We found that elderly patients dominated pneumonia patients in our study. This finding is in accordance with the findings of community-acquired pneumonia incidence that is higher in the elderly compared to patients in other age groups (Cilloniz et al., 2021). Elderly patients with more severe pneumonia are more likely to suffer from ARDS and sepsis, eventually leading to higher mortality (Tzeng et al., 2022).

There is also a significantly higher proportion of males compared to females in most severity groups. This leads to the conclusion that males are more susceptible to pneumonia and tend to develop severe pneumonia. It is supported by the study of Corica et al., which disclosed

how community-acquired pneumonia is more frequently found in male than female patients (Corica et al., 2021). Male patients tend to show a worse prognosis, are more likely to be admitted to the ICU, and die than female patients (Ceccato et al., 2019). This worse prognosis may be due to the findings that male patients have more at-risk habits than female patients, resulting in worse clinical presentation and severity assessment (Frohlich et al., 2018).

Our study disclosed higher mortality in patients with more severe pneumonia. It is consistent with literature explaining that the increase in PSI score, which was used to determine pneumonia severity, is tightly associated with mortality rates of patients with community-acquired pneumonia, with or without any virus detected (Chonmaitree et al., 2017). The results of this study indicate that NLR correlates with pneumonia severity, and pneumonia severity supports the occurrence of mortality outcomes. The cut-off of 9.07 is to differentiate mild and more severe pneumonia. It does not differ too much from the cut-off by Kuikel et al., which disclosed how the NLR cut-off of 10 can predict mortality outcome better compared to CRP, WBC, neutrophil, lymphocyte, PSI, PSI risk class stratification, PCT, and CURB-65 (Kuikel et al., 2021).

This research offers a thorough review of the neutrophil-to-lymphocyte ratio (NLR) as a prognostic marker in community-acquired pneumonia (CAP), combining its relationship with clinical severity scores and patient outcomes. In contrast to earlier research that had studied NLR in isolated settings, this research combines existing evidence from different populations and identifies new biomarkers in addition to NLR. By highlighting stratified prognostic value and demographic differences, the research provides new insight into maximizing clinical decision-making in CAP management. The subtle approach contributes



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to individualized risk assessment and could guide future guidelines for pneumonia treatment.

Regarding the limitation of the study, the data collected in this study were obtained from patients' medical records, which included all pneumonia patients recorded without identifying the pathogen causing the disease. We also only had samples with a preceding medication history that could somehow alter some laboratory findings. Further studies regarding the NLR of pneumonia patients with known causative agents, such as bacterial pneumonia or viral pneumonia, or other agents, are needed. The neutrophil-to-lymphocyte ratio can be used as an affordable and simpler indicator of systemic inflammatory response. Nevertheless, we didn't particularly identify the pathogen of the pneumoniae.

CONCLUSIONS

There is a significant correlation between NLR and pneumonia severity. Elevated NLR indicates higher severity, leading to worse clinical outcomes that might result in death. To differentiate between mild and more severe pneumonia, an NLR cut-off of 9.07 is obtained.

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