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The Relationship Between Platelet to Lymphocyte Ratio (PLR), Monocyte to Lymphocyte Ratio (MLR), Neutrophil to Lymphocyte Ratio (NLR), and Albumin Levels with The Severity of Community-acquired pneumonia (CAP) in Hospitalized Elderly Patients

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ABSTRACT

Background: Community-acquired pneumonia (CAP) is a lung infection that often affects elderly patients and can be severe. Laboratory parameters, including platelet-lymphocyte ratio (PLR), monocyte-lymphocyte ratio (MLR), neutrophil-lymphocyte ratio (NLR), and albumin, have been linked to the prognosis of various infectious diseases. However, the relationship between these parameters and the severity of CAP in elderly patients is not yet fully understood. ***Methods:*** This is an analytic observational study with a cross-sectional design that involved 125 elderly patients (≥60 years old) with CAP who were hospitalized at Prof. Dr. I.G.N.G. Ngoerah Hospital between January and December 2023. The study collected demographic data, nutritional status, smoking status, and laboratory parameters (PLR, MLR, NLR, and albumin) from electronic medical records. The severity of CAP was assessed based on the 2019 IDSA/ATS criteria. Receiver operating characteristic (ROC) analysis was performed to determine the optimal cut-off point of laboratory parameters. Proportion comparison analysis and multivariate logistic regression were used to evaluate the association between laboratory parameters and the severity level of CAP. ***Results:*** Of a total of 125 study subjects, 48 (38.4%) had severe CAP. NLR values ≥9.84 with RR 15.242 (95% CI 4.999-46.475; p<0.001) and albumin values <3.295 g/dL with RR 5.407 (95% CI 2.630-11.115; p<0.001) were significantly associated with the severity of CAP in hospitalized elderly patients. Multivariate analysis showed that NLR had HR 37.426; (95% CI 9.295-150.694; p<0.0001) and albumin had an HR value of 3.747 (95% CI 1.149-12.221; P=0.029) which was significantly associated with the severity of CAP in hospitalized elderly patients after adjusting for confounding factors. ***Conclusions:*** High NLR values and low albumin values may be potential predictors for identifying elderly patients with CAP who are at risk for severity. These findings emphasize the importance of assessing laboratory parameters in managing CAP in the elderly population.

Keywords: CAP; elderly; severity.

INTRODUCTION

Pneumonia is an acute inflammation of the lung parenchyma caused by various pathogens such as bacteria, viruses, fungi, and parasites, excluding Mycobacterium Tuberculosis [1]. It is divided into three main types: Community-acquired pneumonia (CAP), Hospital-Acquired Pneumonia (HAP), and Ventilator-Associated Pneumonia (VAP) [2] CAP is the most common, occurring when the infection is contracted outside of hospitals or in community settings [3]. This condition remains a significant health issue globally, especially in vulnerable populations. Timely diagnosis and treatment are crucial to reduce the risk of severe complications [4]
The elderly population is particularly at risk of severe pneumonia due to factors like aging immune systems and existing comorbidities. Immunosenescence, which is the decline of immune function with age, makes older adults more susceptible to infections [5].

Their clinical symptoms are often atypical, such as confusion or falls, which complicates diagnosis. As a result, pneumonia in the elderly can progress more quickly and lead to higher mortality rates [6]. The presence of multidrug-resistant bacteria also adds to the challenges in managing these patients [7].

To assess the severity of pneumonia, medical professionals often use scoring systems like CURB-65 and the Pneumonia Severity Index (PSI) [8]. However, these tools have limitations, particularly in elderly and immunocompromised individuals. Recent studies have highlighted the use of new inflammatory markers such as Platelet-to-Lymphocyte Ratio (PLR), Monocyte Lymphocyte Ratio (MLR), and Neutrophil Lymphocyte Ratio (NLR). These biomarkers can provide valuable insights into the severity of the disease and patient prognosis. They are also easy to measure and interpret, making them useful in both primary and secondary healthcare settings [6].

Low albumin levels, also known as hypoalbuminemia, have been associated with worse outcomes in elderly patients with pneumonia. Studies show that elderly patients with hypoalbuminemia have lower survival rates compared to those with normal albumin levels. This underscores the importance of early detection and monitoring of inflammatory markers in elderly patients [7]. By using biomarkers like PLR, NLR, MLR, and albumin, clinicians can improve the accuracy of severity assessments. This can ultimately lead to better decision-making in terms of treatment plans and patient care.

METHOD

The research is an observational analytical study with a cross-sectional design. It assesses the severity of CAP in hospitalized elderly patients. At the same time, this study evaluates several laboratory parameters related to the severity of CAP, which include PLR (Platelet-to-Lymphocyte Ratio), MLR (Monocyte-to-Lymphocyte Ratio), NLR (Neutrophil-to-Lymphocyte Ratio), and Albumin.

The inclusion criteria for this study are: elderly individuals aged 60 years and older (Kemenkes RI, 2018) and patients with CAP receiving treatment at RSUP Prof. Dr. I.G.N.G Ngoerah. The exclusion criteria for this study are: 1. Patients with incomplete medical records; 2. Malignancies; 3. Chronic liver disease; 4. Chronic kidney disease with regular hemodialysis; 5. Use of immunosuppressive therapy; 6. Pulmonary tuberculosis; 7. Confirmed COVID-19; 8. Stroke; 9. Acute coronary syndrome; 10. Other sources of acute infection outside the pulmonary organ.

The collected data will be processed to provide the necessary information for the research. After obtaining secondary data, the next step is to enter the data into a computer program. The data will first be transformed into numerical categories (coding) to facilitate data analysis by the software. Data analysis will include descriptive statistics, prevalence comparison tests, and logistic regression tests.

RESULT

In this study, a total of 125 subjects were included, divided into two groups: 48 subjects in the severe CAP group and 77 subjects in the non-severe CAP group. The distribution of the study data was tested using Harman's single-factor test to identify bias, with the result being below 50%. Specifically, the test showed a bias of 35.65%, based on the independent variables studied: PLR, MLR, NLR, and albumin. The characteristics of the data are presented in Table 1

TABLE 1: Characteristics of the Study Subjects (n=125).

Variables	Severity of CAP		p-value
	Severe CAP (n=48)	Non-severe CAP (n=77)	
Age (years)	74 (61-92)	71 (61-98)	0.102[a]
BMI (kg/m2)	***21.18 (14.69-35.63)***	***21.48 (15.63-47.61)***	***0.232[a]***
< 25 kg/m2	35 (72.9%)	45 (58.4%)	0.101[b]
≥ 25 kg/m2	13 (27.1%)	32 (41.6%)	
Gender			
Man	28 (58.3%)	51 (66.2%)	0.373[b]
Woman	20 (41.7%)	26 (33.8%)	
Work			
Work	17 (35.4%)	33 (42.9%)	0.409[b]
Doesn't work	31 (64.6%)	44 (57.1%)	
Smoking Status			
Yes	28 (58.3%)	36 (46.8%)	0.208[b]
No	20 (41.7%)	41 (53.2%)	
Laboratory results			
PLR	201.28 (13.82-825.71)	212.24 (16.22-933.33)	0.943[a]
MLR	0.89 (0.04-3.45)	0.67 (0.06-3.85)	0.235[a]
NLR	21.83 (1.83-40.09)	5.61 (0.01-18.49)	<0.001[a]*
Albumin	2.88±0.44	3.48±0.60	<0.001[c]*

[a] Uji Mann-Whitney; [b]Chi-square test; [c]uji Independent t;*Significant p<0,05.

The ROC curve results presented in Figure 1 showed an area under the curve (AUC) value of 0.504 (95% CI 0.395-0.612; p=0.943), with a sensitivity of 50.0% and a specificity of 49.4%, indicating a PLR threshold value of 211.68.

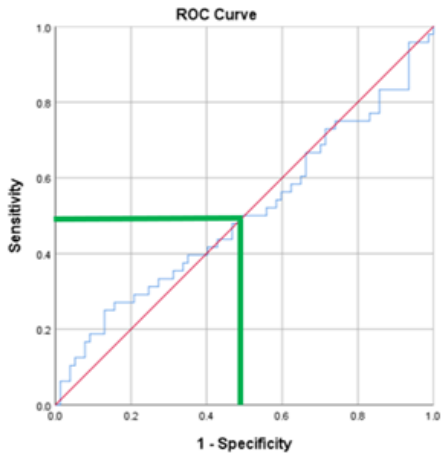

FIGURE 1: ROC Curve of PLR influencing severe CAP.

The results of the bivariate analysis are presented in Table 2, which shows that high PLR levels in patients with severe CAP were not significantly associated (p=0.621).

TABLE 2: Risk of severe CAP in patients with high PLR (≥211.68) compared to those with low PLR.

Variables	Severity of CAP		RR	IK 95%	p-value
	Severe CAP	Non-severe CAP			
High PLR ≥211.68	24 (40.7%)	35 (59.3%)	1,119	0.718-1.743	0.621
Low PLR <211.68	24 (36.4%)	42 (63.6%)			

*Chi-square test signifikan p<0,05; PLR: Platelet Limfosit Ratio; RR: Relative risk.

The ROC curve results presented in Figure 2 showed an area under the curve (AUC) value of 0.563 (95% CI 0.456-0.671; p=0.235), with a sensitivity of 58.3% and a specificity of 57.1%, indicating an MLR threshold value of 0.749.

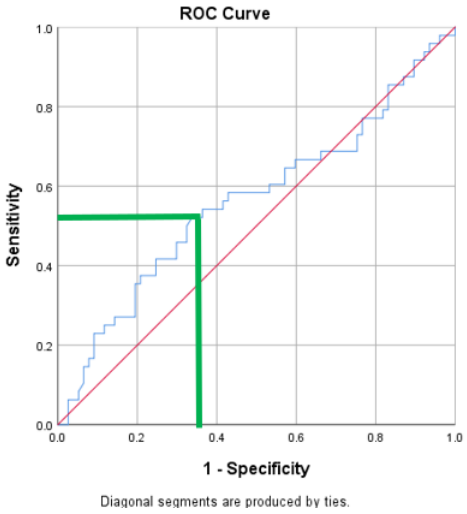

FIGURE 2: ROC Curve of MLR influencing severe CAP.

A bivariate analysis is presented in Table 3, which shows that high MLR levels in patients with severe CAP were not significantly associated (p=0.092).

TABLE 3: Risk of severe CAP in patients with high MLR (≥0.749) compared to those with low MLR.

Variables	Severity of CAP		RR	IK 95%	p-value
	Severe CAP	Non-severe CAP			
High MLR ≥0.749	28 (45.9%)	33 (54.1%)	1,469	0.933-2.313	0.092
Low MLR<0.749	20 (31.3%)	44 (68.8%)			

*Chi-square test significant; MLR: Monosit Limfosit Ratio.

The ROC curve results are presented in Figure 3 an AUC value of 0.984 (95% CI 0.903-0.992; p<0.001), with a sensitivity of 93.8% and a specificity of 87.9%, indicating an NLR threshold value of 9.84.

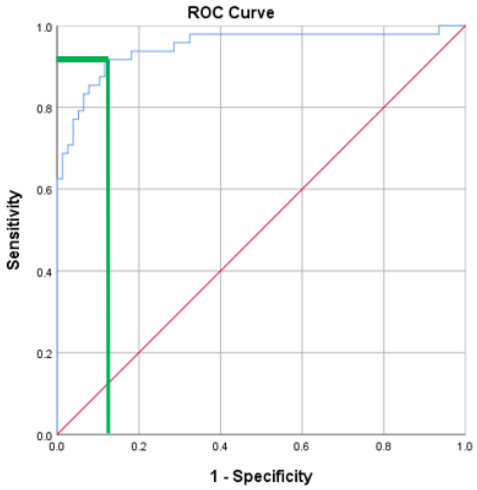

FIGURE 3: ROC Curve of NLR influencing severe CAP.

A bivariate presented in Table 4 that high NLR compared to those with low NLR (72.6% vs. 4.8%; p<0.001). Patients with high NLR (≥9.84) were found to have a significantly higher risk 15.242 times (95% CI 4.999-46.475; p<0.001).

TABLE 4: Risk of severe CAP in patients with high NLR (≥9.84) compared to those with low NLR.

Variables	Severity of CAP		RR	IK 95%	p-value
	Severe CAP	Non-severe CAP			
High NLR ≥9.84	45 (72.6%)	17 (27.4%)	15.42	4.999-46.475	<0.001*
Low NLR<9.84	3 (4.8%)	60 (95.5%)			

*Chi-square test significant; NLR: Neutrofil Limfosit Ratio.

The ROC analysis showed an area under the curve (AUC) value of 80.1% (95% CI 0.723-0.878; p<0.001), with a sensitivity of 87.5% and a specificity of 70.1%, indicating an albumin threshold value of ≤3.295 (Figure 4).

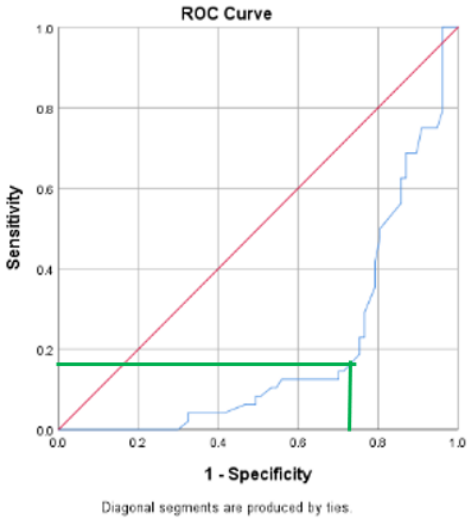

FIGURE 4: ROC Curve of albumin influencing severe CAP.

A bivariate analysis are presented in Table 5, which shows that low albumin levels were more frequently associated with severe CAP compared to higher albumin levels (63.1% vs. 11.7%; p<0.001). Patients with low albumin (≤3.295) were found to have a significantly higher risk—5.407 times more likely—of developing severe CAP (95% CI 2.630-11.115; p<0.001).

TABLE 5: Risk of severe CAP in patients with low albumin (≤3.295) compared to those with high albumin.

Variables	Severity of CAP		RR	IK 95%	p-value
	Severe CAP	Non-severe CAP			
Low albumin ≤3.295	41 (63.1%)	24 (36.9%)	5,407	2,630-11,115	<0.001*
High albumin >3,295	7 (11.7%)	53 (88.3%)			

*Chi-square test significant p<0,05.

The multivariate analysis was conducted using logistic regression with the backward LR method (Table 6) showed that NLR had a hazard ratio (HR) of 37.426 (95% CI 9.295-150.694; p<0.0001), and for albumin, the HR was 3.747 (95% CI 1.149-12.221; p=0.029).

TABLE 6: Logistic regression results using the backward LR method.

Variables	HR	IK95%		p* value
		Lower limit	Upper limit	
Step 1				
PLR	1,506	0.409	5,549	0.539
MLR	2,156	0.627	7,417	0.223
NLR	38,096	8,837	164,236	0,000
Albumin	3,736	1,076	12,972	0.038
Gender	0.583	0.120	2,844	0.505
Work	1,026	0.323	3,260	0.966
IMT	3,711	1,049	13,130	0.042
Smoking status	1,853	0.383	8,973	0.444
Step 6				
NLR	37,426	9,295	150,694	<0.001*
Albumin	3,747	1,149	12,221	0.029*
IMT	2,924	,949	9,004	0.062

*logistic regression analysis significant.

DISCUSSION

This study involved 125 patients diagnosed with CAP, comprising 48 with severe pneumonia and 77 with non-severe pneumonia. These findings align with Maranatha and Mawardi (2019) in Indonesia, who reported 39 severe and 41 non-severe cases among 80 patients. The higher number of non-severe cases in this study might be attributed to elderly patients with CAP who had other medical conditions such as infections or comorbidities, disqualifying them from the severe category [9]. Similarly, Cillóniz et al. (2013) studied 2,149 elderly patients (>65 years) with CAP, where 1,467 (68.3%) were classified as non-severe and 682 (31.7%) as severe, based on the CURB-65 score [10]. Non-severe pneumonia in elderly patients is often linked to atypical symptoms, underdiagnosis, and comorbidities, which can obscure pneumonia's severity. Increased life expectancy and advancements in medical care have also led to a higher proportion of CAP cases among the elderly [11].

Aging is associated with physiological changes and immune function decline, making older individuals more susceptible to bacterial infections. Studies have found a correlation between advanced age and increased severity of CAP. Ghia and Rambhad (2022) identified age ≥50 years as a significant risk factor for CAP, with a prevalence of 55.8% among patients, highlighting the vulnerability of older populations to CAP, leading to higher morbidity and mortality [12].

Regarding Body Mass Index (BMI), most patients in this study had a BMI below 25 kg/m^2. BMI is critical in the prognosis of CAP, as both underweight and obese individuals are at greater risk of complications compared to those with a normal BMI. Underweight individuals tend to have weaker immune systems, making them more vulnerable to infections, while obesity is linked to chronic inflammation, which can worsen pneumonia. Research indicates that BMI significantly enhances the prognostic value of N-terminal pro-B-type natriuretic peptide (NT-proBNP) in pneumonia patients[13,14].

In terms of gender distribution, this study found no statistically significant difference between males and females in terms of CAP severity. However, other studies suggest that males are more likely to develop

pneumonia due to biological, behavioral, and environmental factors such as smoking and occupational hazards, which increase the risk of pneumonia [15].

Employment status also showed no significant correlation with CAP severity. Similarly, the study found no significant difference in smoking status between severe and non-severe cases. These findings are consistent with Almirall et al. (2014), which noted that smoking does not always have a linear relationship with pneumonia risk, as other factors like environmental exposure and weakened immune systems can contribute to the disease [16].

Research consistently demonstrates that NLR is a reliable marker for predicting the severity of CAP. In this study, patients with NLR values greater than 9.84 had a significantly higher risk of developing severe pneumonia. This is in line with studies like Liu et al. (2023), which found that elevated NLR is an independent factor associated with pneumonia severity in elderly patients [17]. The study reported that an increase in NLR was significantly correlated with disease severity, with an AUC (Area Under the Curve) of 0.817 for predicting pneumonia severity. The odds ratio for NLR predicting severe pneumonia was 1.111, showing that for each unit increase in NLR, the risk of severe pneumonia rose proportionally. Similar findings were echoed by Yang et al. (2020) during the COVID-19 pandemic, where higher NLR values were strongly linked with disease severity [18].

Furthermore, NLR reflects the balance between neutrophils and lymphocytes, two key components of the immune response. Elevated neutrophil counts indicate increased inflammation, while decreased lymphocyte counts suggest a weakened adaptive immune response, making NLR a useful marker for detecting the body's overall immune status. A high NLR is indicative of an exaggerated inflammatory response, which can lead to complications such as severe lung damage, multi-organ failure, and a higher risk of mortality. This makes NLR a valuable prognostic tool in managing pneumonia, particularly among elderly patients who are more prone to severe outcomes [17,19,20].

Similarly, albumin levels are a critical marker in assessing pneumonia severity. Albumin, a major protein in the blood, plays multiple roles, including maintaining oncotic pressure and acting as an antioxidant. This study found that patients with albumin levels ≤3.295 g/dL had a significantly higher risk of severe pneumonia. Several studies, such as Damayanti et al. (2018) and Abdeen et al. (2021), have demonstrated that low albumin levels are associated with a higher risk of 30-day mortality in CAP patients [21,22]. Abdeen's study showed that patients who died in the hospital had significantly lower albumin levels compared to those who survived, reinforcing the importance of hypoalbuminemia as a mortality predictor [21].

The mechanism of low albumin levels and pneumonia severity can be attributed to the role of albumin in inflammatory regulation and nutritional status. Hypoalbuminemia often reflects malnutrition or chronic illness, both of which weaken the immune system and impair the body's ability to fight infections. Moreover, low albumin levels can indicate systemic inflammation, as proteins are broken down more rapidly during an inflammatory response, thus exacerbating disease severity. Therefore, albumin serves not only as a nutritional marker but also as an indicator of the body's capacity to withstand severe infections like pneumonia [23–25].

On the other hand, PLR and MLR did not significant relationship with pneumonia severity in this study. PLR, which measures the ratio of platelets to lymphocytes, did not correlate significantly with severe CAP, as indicated by the p-value of 0.943 in this study. This finding is consistent with research by Ng et al. (2022) and Yang et al. (2020), which reported that while PLR might be elevated in severe infections, it lacks the sensitivity and specificity required to reliably predict pneumonia outcomes [18,26].

One explanation for this lack of significance is that platelet counts do not always correlate directly with the intensity of lung infections. While platelets participate in the inflammatory process by releasing cytokines and chemokines, their count can be influenced by various factors unrelated to pneumonia severity. Additionally, platelets are regulated by thrombopoiesis in the bone marrow, and their consumption in tissues during infections might not accurately reflect the severity of the infection. As a result, PLR may not be as reliable a marker for pneumonia severity as other ratios, such as NLR [17,18,27].

Similarly, MLR, which compares monocytes to lymphocytes, did not show a significant association with CAP severity, as seen in the p-value of 0.235. Studies by Ng et al. (2022) and Cui et al. (2023) found no significant diagnostic value for MLR in predicting pneumonia severity or mortality [26,28]. The variability in monocyte counts, which depend on factors like infection stage and monocyte mobilization, makes MLR less specific for determining lung infection severity. Monocytes play a role in the innate immune response, particularly through phagocytosis and the release of pro-inflammatory cytokines, but this response is not always proportional to infection severity. Therefore, MLR might not effectively capture the adaptive immune responses crucial in determining pneumonia severity.

These study findings suggest that routine monitoring of NLR and albumin could improve the management and prognosis of elderly CAP patients. Further research, particularly multi-center studies, is needed to confirm these findings and explore additional factors influencing CAP severity in this population.

CONCLUSION

Based on the research findings, it can be concluded that a high NLR value and low albumin levels are significantly associated with greater severity of CAP

in elderly inpatients. In contrast, high PLR and MLR values do not show a significant relationship with the severity of pneumonia.

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