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The Relationship Between D-Dimer and NLR With the Clinical Severity of Pneumonia in Covid-19 Patients at the Regency Hospital Sidoarjo Period of June to August 2021

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ABSTRACT
COVID-19 has a wide range of severity categorized ranging from asymptomatic to critical symptoms, with varying clinical indicators such as pneumonia and hypoxia. This severity can be predicted using a variety of parameters, including neutrophil-to-lymphocyte ratio (NLR) and D-dimer levels, which are important prognosis markers in assessing disease progression. This study aims to determine the relationship between NLR and D-dimer with the clinical severity of pneumonia in COVID-19 patients at Sidoarjo Regency Hospital in the period of June to August 2020. The research method used is observational using secondary data from the electronic medical records of Sidoarjo Regency Hospital. Data analysis was carried out using the Kruskal-Wallis statistical test. The study population included all patients diagnosed with pneumonia due to COVID-19 and treated at Sidoarjo Regency Hospital, while the sample included patients who had complete data for NLR and D-dimer.

Keywords: *D-Dimer, Parameters, Covid-19*

1. INTRODUCTION

The Covid-19 pandemic has had an effect on all countries in the world. Indonesia is one of the countries affected by this pandemic. According to data per July 27, 2020, the number of confirmed cases in Indonesia is 100,303 cases. East Java is the second largest contributor to the number one case in Indonesia after DKI Jakarta (Covid-19 Team Data, 2020). The study conducted by Tigist W. Leulseged et al., on 429 patients, reported that 182 (42.4%) were admitted to the hospital with severe clinical conditions and the remaining 247 (57.6%) were admitted to the hospital with mild clinical conditions. It was reported about the Prognosis of Patients in the Tigist W. Leulseged Study et al. (10.5%) were discharged from the hospital in a state of death, while the remaining 384 (89.5%) went home in a condition of recovery from Covid-19. Laboratory results were as follows (ARR = 1,779, 95%CI = 1,405–2,252, p-value <0.0001), Neutrophil to Lymphocyte ratio (NLR) (ARR = 4,769, 95% CI = 2,419– 9,402 p-value <0.0001), Serum glutamic oxaloacetate transaminase (SGOT) (ARR = 1,358, 95%CI = 1,109–1,662 p-value = 0.003), Sodium (ARR = 1,321, 95%CI = 1,091–1,600 p-value = 0.004) and Potassium (ARR = 1,269, 95% CI = 1,059–1,521 pvalue = 0.010) was found to be a significant predictor of COVID-19 severity.

The research conducted by Gong et al., on producing a tool for early prediction of severe COVID-19 pneumonia from the following data: age, serum LDH activity, C reactive protein (CRP), coefficient of variation in the width of red blood cell distribution, blood urea nitrogen, diurea bilirubin, low albumin. The resulting performance is not very high (sensitivity 77.5%, specificity 78.4%). This is suspected because the data used as input consists of age and laboratory findings. Several studies were conducted by various researchers from various countries, motivating us to find out the relationship between D-Dimer and NLR with the degree of clinical severity of pneumonia in Covid-19 patients at Sidoarjo Regency Hospital for the period of June to August 2020.

2. MATERIAL AND METHODS

Types of research

This type of research is observational research with data sources from the Electric Medical Records of the Hospital Sidoarjo Regency with Statistical Test Data Analysis using Kruskall allis.

Research population and sample

The population in this study all patients diagnosed with Pneumonia due to Covid19 are treated at Sidoarjo Regency Hospital with sample of all patients diagnosed as Covid-19 Month period June to August 2020 treated at Sidoarjo Regency Hospital has DL data (NLR) and D-dimer.

3. RESULT

This study analyzed the relationship between NLR and D-dimer and the clinical severity of pneumonia in COVID-19 patients treated at Sidoarjo Regency Hospital during the period from June to August 2020. A total of 327 patients diagnosed with pneumonia due to COVID-19 were included in this study.

The Relationship of NLR to the Severity of COVID-19

The results of the analysis showed that there was a significant relationship between NLR and the severity of COVID-19. Of the 327 patients, those with an NLR of > 3.13 were more likely to experience severe to critical symptoms (p = 0.018). A total of 64.0% of patients with moderate severity and 85.7% with severe or critical severity had an NLR > 3.13, suggesting that increased NLR correlates with increased disease severity. This can be seen in Table 1. and Figure 1 below:

Table 1. NLR Crosstab and COVID-19 Severity

			Severity			Total
			Moderate severity	Severity of weight	Critical	
nlr	NLR <=3.13	Count	62	1	33	96
		Expected Count	50.5	2.1	43.4	96.0
		% within nlr	64.6%	1.0%	34.4%	100.0%
		% within keparahan	36.0%	14.3%	22.3%	29.4%
		% of Total	19.0%	0.3%	10.1%	29.4%
	NLR > 3.13	Count	110	6	115	231
		Expected Count	121.5	4.9	104.6	231.0
		% within nlr	47.6%	2.6%	49.8%	100.0%
		% within keparahan	64.0%	85.7%	77.7%	70.6%
		% of Total	33.6%	1.8%	35.2%	70.6%
Total		Count	172	7	148	327
		Expected Count	172.0	7.0	148.0	327.0
		% within nlr	52.6%	2.1%	45.3%	100.0%
		% within keparahan	100.0%	100.0%	100.0%	100.0%
		% of Total	52.6%	2.1%	45.3%	100.0%

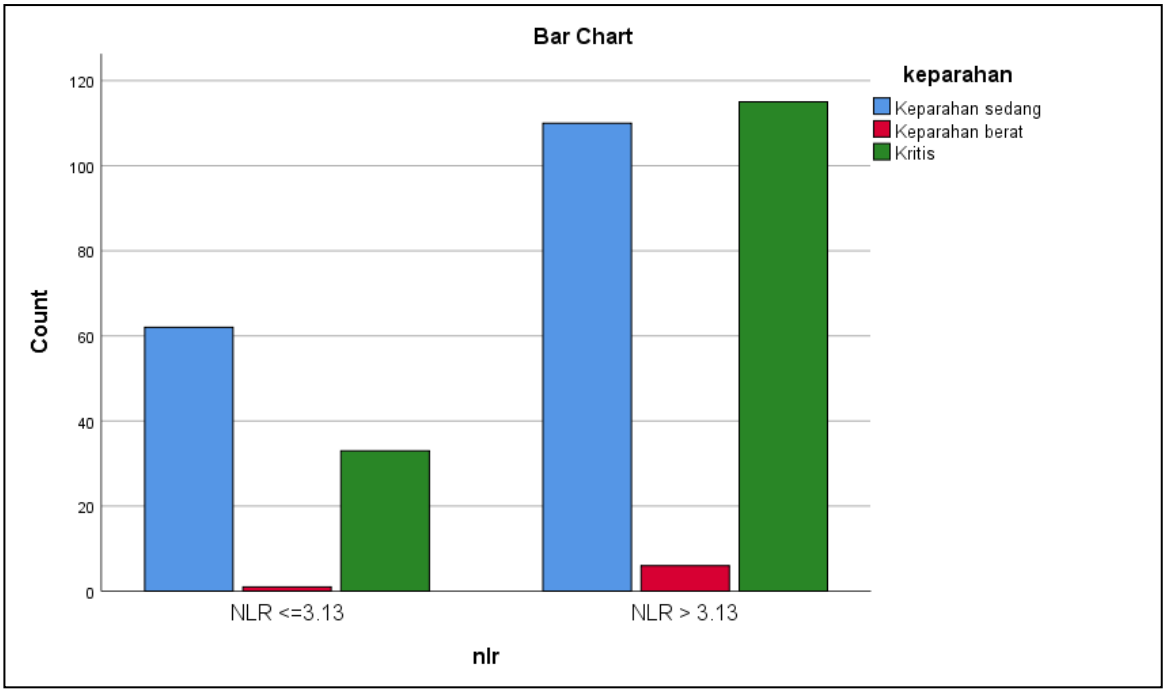

Figure 1. Graph of the Relationship of NLR to the Severity of COVID-19

Table 2. Chi-Square analysis results

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	8.035[a]	2	.018
Likelihood Ratio	8.202	2	.017
Linear-by-Linear Association	7.281	1	.007
N of Valid Cases	327		

a. 2 cells (33.3%) have expected count less than 5. The minimum expected count is 2.06.

This table shows the relationship between NLR (≤3.13 and >3.13) and severity (moderate, severe, critical). An important result was that patients with an NLR of > 3.13 tended to experience more severe to critical symptoms, with a significant value of p = 0.018.

Relationship of D-dimer with COVID-19 Severity

From the analysis of D-dimer levels, it was found that D-dimer levels > 500 were also significantly related to the severity of COVID-19 (p = 0.002). Patients with D-dimer levels > 500 are more likely to experience critical symptoms, with 64.2% of critical patients having high D-dimer levels. This can be seen in Table 3. and Figure 2. below

Table 3. Crosstab D-dimer and Severity of COVID-19

			Severity			Total
			Moderate severity	Severity of weight	Critical	
ddimer	NOT <= 500	Count	91	1	53	145
		Expected Count	76.3	3.1	65.6	145.0

		% within ddimer	62.8%	0.7%	36.6%	100.0%
		% within keparahan	52.9%	14.3%	35.8%	44.3%
		% of Total	27.8%	0.3%	16.2%	44.3%
	NOT > 500	Count	81	6	95	182
		Expected Count	95.7	3.9	82.4	182.0
		% within ddimer	44.5%	3.3%	52.2%	100.0%
		% within keparahan	47.1%	85.7%	64.2%	55.7%
		% of Total	24.8%	1.8%	29.1%	55.7%
Total		Count	172	7	148	327
		Expected Count	172.0	7.0	148.0	327.0
		% within ddimer	52.6%	2.1%	45.3%	100.0%
		% within keparahan	100.0%	100.0%	100.0%	100.0%
		% of Total	52.6%	2.1%	45.3%	100.0%

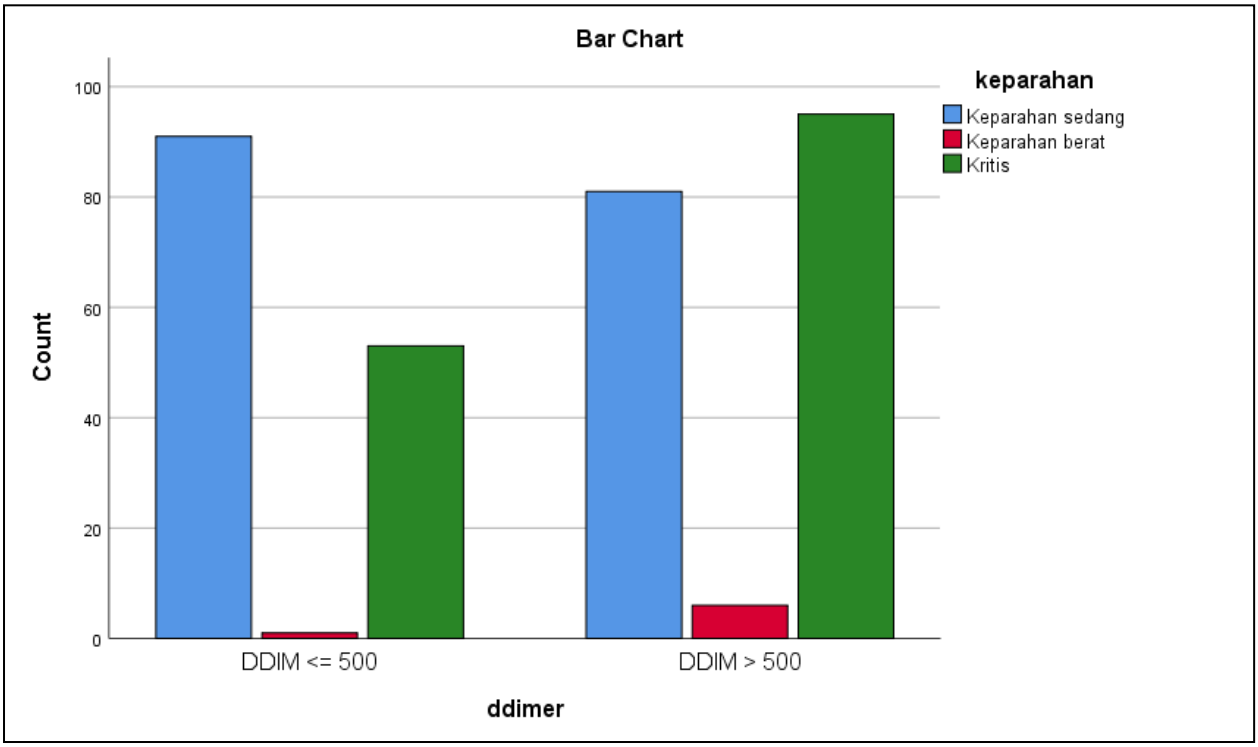

Figure 2. Graph of the Relationship of D-dimer and Severity of COVID-19

Table 2. Chi-Square analysis results

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	12.039[a]	2	.002
Likelihood Ratio	12.433	2	.002
Linear-by-Linear	9.500	1	.002

Association	
N of Valid Cases	327

a. 2 cells (33.3%) have expected count less than 5. The minimum expected count is 3.10.

This table shows the distribution of patients based on D-dimer levels (≤500 and >500) of the same severity. The results showed that patients with D-dimer > 500 were more likely to experience critical symptoms, with a significant value of p = 0.002.

4. DISCUSSION

NLR is an available biomarker that can calculate the white blood cell count component (dividing neutrophils by lymphocyte count). NLR or Neutrophil Lymphocyte Ratio is one of the necessary parameters for the prognosis of infection, inflammation and some types of cancer. Netrophils themselves serve as a defense against microbial invasion or phagocytosis. These cells have an important role in the diagnosis of inflammation and infection. Meanwhile, Lymphocytes are small cells that move to the inflammatory region. Lymphocytes are also an important source of immunoglobulins in the body's cellular immune response. Lymphocytes have a role to fight infections caused by viruses or bacteria.

D-dimer is a fragment produced when plasmin breaks down fibrin to break down blood clots. This examination is routinely used as part of the diagnosis algorithm to rule out the diagnosis of thrombosis. However, pathological or non-pathological processes that increase fibrin production or its breakdown, can also increase plasma levels of D-dimers. Plasma levels of D-dimer, Fibrin Degradation Product (FDP), almost always increase with the presence of Pulmonary Embolism (PE). Therefore, normal D-dimer levels (below the limit value of 500 micrograms/L.

5. CONCLUSION

In this study, the increase in **NLR value** is a determining factor that ensures that clinically the patient's condition deteriorates. This is in line with the increased value of D-dimer which is a fragment produced when plasmin breaks down fibrin to decompose. Blood clots are a determining factor in the occurrence of thrombosis (pulmonary embolism). Conclusion that the Improvement of Both Factors of both NLR & D-Dimer ensures that the state of Pneumonia sufferers due to COVID-19 has a poor prognosis.

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