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Original Article

Correlation Procalcitonin (PCT) to Neutrophil Lymphocyte Ratio (NLR) in Covid-19 Patient

Isnawati Apriliani[1], Rizana Fajrunni'mah[1], Husjain Djajaningrat[1], Aninda Dinar Widiantari[2], Farida Murtiani[2]

[1]Department of Medical Laboratory Technology, Health Polytechnique of Jakarta III Jakarta, Indonesia
[2]Research Installation, Sulianti Saroso Infectious Disease Hospital Jakarta, Indonesia

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Author Affiliation:
Research Installation,
Sulianti Saroso Infectious Disease Hospital
Jakarta, Indonesia

Author Correspondence:
Farida Murtiani
Sunter Permai Raya Street. No.2,
Jakarta 14340, Indonesia

E-mail:
Idoel_fh@yahoo.com

Abstract

Background : Covid-19 treatment should be done early before the disease progress. Inflammatory biomarker is needed to ascertain the severity of disease as soon as possible. Neutrophil-to-lymphocyte ratio (NLR) and Procalcitonin (PCT) are two of biomarker that are clinically used around the world. NLR is simpler, can routinely be done and available in peripheral region while PCT is more effective to describe inflammation. This study aims to determine the correlation of procalcitonin (PCT) levels with neutrophil lymphocyte ratio (NLR) in COVID-19 patients.
Methods : This study is an analytic observational with a cross sectional design. We extracted data from medical record. Samples were 415 COVID-19 patients undergoing inpatient care at the Budhi Asih Hospital, East Jakarta for January - December 2021.
Results: Prevalence of male patients more than ≥60 years were 78 patients (18.8%) while female patients were 68 patients (16.4%). Average of PCT level was 1,93 ng/mL (0.02–200 ng/mL). Average of NLR was 5.09 cells/mm3 (0.22–31 cells/mm^3). Spearman test proved there was a significant correlation between PCT and NLR levels in COVID-19 patients (p value = 0.0001).
Conclusion: The higher the PCT level, the higher the NLR value in COVID-19 patients.

Keywords : COVID-19, Procalcitonin (PCT), Neutrophil Lymphocyte Ratio (NLR)

INTRODUCTION

Coronavirus Disease 2019 is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection. On March 11, 2020, WHO declared the phenomenon as a Public Health Emergency of International Concern (PHEIC) and a pandemic. In severe cases of COVID-19, it leads to an acute respiratory syndrome problem, pneumonia, kidney failure, and even to death.[1]

According to recommendation by WHO, gold standard of COVID-19 diagnosis is a biomolecular examination called real-time-PCR (qPCR). Samples in the form of RNA will be converted into cDNA in the form of a single strain and will be detected in real time.[2]

The presence of inflammatory in COVID-19 patients can be detected using procalcitonin (PCT) examination. PCT is a serological indicator in the shape of prohormones that are increasingly being studied for their role as a determinant of etiology in infectious diseases. Compared to other inflammatory parameters, such as CRP, PCT generally provides better sensitivity and specificity. After sensitization by bacterial stimuli, PCT levels also increase faster compared to CRP.[3]

In COVID-19 case, PCT help distinguishing between severe bacterial pneumonia and mild viral pneumonia. PCT level examination is an important test in identifying COVID-19 patients who are at high risk, have clinical aggravation, and patients with bacterial co-infection.[4] However, the PCT parameter has several disadvantages, such as high cost, long examination time, thus it is not widely available in health facilities in Indonesia.[5]

To detect inflammation in COVID-19 case, we also perform Neutrophil Lymphocyte Ratio (NLR) examination. Patients with severe SARS-CoV-2 infection are often characterized by neutrophilia that follows lymphopenia.[4] NLR is obtained from the comparison of neutrophil and lymphocytes.[6] Compared to PCT, NLR examination are easier to get, cheaper, non-invasive, and can be done more regularly.[7,8]

In previous studies, a similar analysis of PCT and NLR levels in Covid-19 case had been carried out. However, the study has limitation due to a small number of samples (n=5), so further research is needed on "Correlation of Procalcitonin Levels (PCT) with Neutrophil Lymphocyte (NLR) Ratio in COVID-19 Patients."

METHODS

This study was an analytical observational study with cross-sectional design. We collected data from medical records. This research was conducted in Budhi Asih Hospital in April–June 2022 and had been approved by ethic committee by issuing a letter number: 56/KEP-ETIK/III/2022. The samples were confirmed COVID-19 patients who admitted inpatient wards in the hospital with total sampling method. We performed analyzing using SPSS software. Spearman test was used to demonstrate correlation of PCT and NLR.

RESULTS

We collected 415 samples. The results showed most patients were male, older than 60 years old (Table 1).

Total average level of PCT was 1.93 ng/mL (0.02-200 ng/mL), while average level of NLR was 5.09 cells/mm^3 (0.22–31 cells/mm^3) (Table 2).

There were 73 (17.6%) patients with high NLR level and high PCT levels. Based on the results of the Spearman rank correlation analysis, with a confidence level of 95% ($\alpha = 0.05$), it was obtained p-value was equal to 0.0001, which meant a significant correlation between PCT and NLR levels (Table 3).

DISCUSSION

Our results showed that male, older than 60 years old (n=78; 18.8%) was more likely to undergo hospitalization compared to female in similar age group (n=68; 16.4%). Elderly patients experience a degenerative period causing decrease of immune response thus they will be more susceptible to infectious diseases and easily infected by SARS COV-2. In addition, female have more dominant immune system than male due to the influence of X chromosome, thus male might be more susceptible to COVID-19 than female.[9–12]

In this study, average PCT level was 1.93 ng / mL (0.02 ng / mL – 200 ng / mL). PCT level can reach up to more than 100 ng/mL in severe infection that manifest to clinical symptoms.[13] In viral infection, PCT shall not be induced as it is initiated by inflammation marker caused by bacterial infection. Increasing level of PCT was in line to severity of diseases.[14] The increase in PCT values occurs approximately 2 hours after exposure and sensitization of microbes. Peak PCT levels occur after 12–48 hours and then decrease.[15]

In this study, the average of NLR value was 5.09 cells/mm^3 (0,22 cells/mm^3 – 31 cells/mm^3). Inflammation caused by the virus resulted an increase in NLR level and induce worse symptoms.[16] Neutrophil work actively by migrating to immune system or organ.[17] Lymphocytes play a role in the process of maintaining homeostasis and inflammatory responses in the body. One of the characteristics of viral infection is occurrence of lymphopenia so that number of lymphocytes can be used as a reference index in the diagnosis of COVID-19 infection.[4,18] NLR is a combination of two parameters. An increase in neutrophil values indicates the presence of systemic inflammation while lymphopenia describes the sequestration of lymphocytes on the inflammatory site

TABLE 1
Respondents' Characterisitic based on Age and Gender

Variable		Gender				Total	
		Male		Female			
		n	%	n	%	n	%
Age (Years)	≥60	78	18.8	68	16.4	146	35.2
	50–59	60	14.5	58	14	118	28.4
	40–49	27	6.5	35	8.4	62	14.9
	30–39	30	7.2	22	5.3	52	12.5
	20–29	9	2.2	15	3.6	24	5.8
	6–19	5	1.2	6	1.4	11	2.7
	≤5	2	0.5	0	0	2	0.5
	Total	211	50.8	204	49.2	415	100

TABLE 2
Level of PCT and NLR

Variable	Average	Minimal	Maximal
PCT (ng/mL)	1.93	0.02	200
NLR (cells/mm^3)	5.09	0.22	31

TABLE 3
Cross Tabulation PCT and NLR

Variable		PCT level						p value
		High	%	Normal	%	Total	%	
NLR level	High	73	17,6	191	46	264	63.6	0.0001
	Normal	10	2,4	141	34	151	36.4	
Total		83	20	332	80	415	100	

and its apoptosis process.[19]

In this study, a positive correlation was found between PCT and NLR, which means both PCT and NLR could be used as an indicator of inflammation in COVID-19 case.[20,21] In line to Wang *et al*.[10,22] which stated there was a positive correlation between PCT and NLR in COVID-19 case. Xu *et al*. in their study found tendency of high level of PCR and NLR was simultaneously to severity and followed by other biomarkers such as CRP.[10] This suggested that NLR level was sufficient to represent inflammatory condition without the need for another biomarker examination, unless there was another indication.

In our study, there were 73 (17.6%) patients with high NLR level and high PCT level. These results were possibly due to inflammation response followed by bacterial co-infection. There were 191 (46%) case with high level of NLR and normal PCT level, this might be due to inflammation response in covid-19 without bacterial co-infection. Limitations of the study was there was no confirmation of bacterial co-infection. We suggested to enclose microbiological culture regarding this matter in the future study.

CONCLUSION

We found a significant correlation between procalcitonin (PCT) levels and ratio of neutrophil lymphocytes (NLR) in COVID-19 patients. The results of this study could be used as recommendations for clinicians in determining laboratory examination in COVID-19 patients.

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