Vol. 5 No. 1 Year 2024
jurnal.umj.ac.id/index.php/MMJ
mmjfkk@umj.ac.id
e-issn: 2721–317X
Muhammadiyah Medical Journal

Research Article

Correlation between Neutrophil to Lymphocyte Ratio with C-Reactive Protein Levels in COVID-19 Patient

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ABSTRACT

Background: *Coronavirus* Disease 2019 (COVID-19) is an infectious disease brought on by SARS-CoV-2. China's Hubei Province's Wuhan City is where the pandemic first began. The number for Indonesia is 1,790. Neutrophil Lymphocyte Ratio (NLR) and C-reactive protein (CRP) tests are conducted to assess the disease prognosis in COVID-19 patients, who may have a bad prognosis. **Purposes:** To find out the relationship between NLR and CRP in COVID-19 patients at Bunda Margonda General Hospital in 2021. **Method:** This study used an analytic observational method with a cross-sectional approach and used secondary data from 100 samples from COVID-19 patients' medical records at Bunda Margonda General Hospital in 2021. **Results:** More COVID-19 patients were found in 56 male patients, aged 46-55 years, with 22 patients; NLR values increased in 67 patients and 80 patients in CRP. There is a significant relationship between NLR and CRP in COVID-19 patients at Bunda Margonda General Hospital in 2021, with a *p-value* of 0.001. The most common COVID-19 cases were found in male patients 46-55 years of age, and there was an increase in the NLR and CRP values. **Conclusion:** There is a relationship between NLR and CRP in COVID-19 patients at Bunda Margonda General Hospital in 2021.

Keywords: covid-19, c-reactive protein, neutrophil lymphocyte ratio

INTRODUCTION

The infectious agent causing Coronavirus Disease 2019 (COVID-19), which affected over six million people globally in March 2022, is the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). The pandemic started in China's Wuhan City of Hubei Province (1). Indonesia is the fourth most populous country in the world. As of April 2, 2020, Indonesia has reached 1,790 confirmed cases, 113 new cases, 112 recoveries, and 170 deaths. Fever (88.7%), cough (67.8%), fatigue (38.1%), sputum production (33.4%), dyspnea (18.6%) %, sore throat (13.9%), and headache (13.6%) were the most prevalent symptoms reported by COVID-19 patients. Some cases have spontaneous recovery (2).

While the majority of adult COVID-19 patients have a good prognosis, those with chronic illnesses over 60 years of age who have a poor prognosis may have severe pneumonia, acute respiratory distress syndrome, pulmonary edema, multiple organ failure, or even death.

Hematological changes caused by viruses can be numerous. Research has demonstrated that COVID-19 patients frequently experience lymphopenia (1,3,4). Consequently, it has been proposed that the neutrophil-to-lymphocyte ratio (NLR) in peripheral blood can help differentiate between different infection types and forecast how an infection would turn out (5,6). CRP, one of the most sensitive acute phase reactants, is practically nonexistent in the serum of healthy individuals and is a well-known indication of inflammation. CRP levels can increase significantly after severe trauma, inflammation, and bacterial and viral infections (7). Additionally, elevated CRP levels have been noted in COVID-19 individuals (4). The use of c-reactive protein levels and the neutrophil-lymphocyte ratio as indicators of the severity and prognosis of illness has been documented internationally (8). This research intends to find the link between NLR and CRP in COVID-19 patients at Bunda Margonda General Hospital in 2021.

METHODS

This study was carried out at Bunda Margonda General Hospital using a cross-sectional method and quantitative analysis. The sample selection in this study used the total sampling method. Namely, the researcher took all data on COVID-19 patients in 2021. The total population in this study was 100 samples that met the inclusion criteria. Therefore, the sample used in this study was 100 samples. The variables of this study were age, sex, and the value of the ratio of neutrophil lymphocytes to C-reactive protein levels in patients confirmed with COVID-19 at Bunda Margonda General Hospital in 2021. The inclusion criteria in this study were patients with complete medical records over or equal to 18 years who were confirmed with COVID-19 in 2021 and had NLR and CRP examination records. Age classification: late teens (17–25 years), early adults (26–35 years), late adults (36–45 years), early seniors (46–55 years), late seniors (56–65 years), and seniors (seniors) >65 years. NLR is expected when the result is < 3.13, and CRP is Normal when < 0.3 mg/dL. The spearmen correlation test used SPSS statistical analysis program 26 version. This study has received a letter of ethics assessment from the Health Research Ethics Commission Faculty of Medicine and Health, Universitas Muhammadiyah Jakarta, number 297/PE/KE/FKK-UMJ/XI/2022.

RESULTS

Table 1. shows that the distribution based on age found patients with confirmed COVID-19 at Bunda Margonda General Hospital in 2021 showed that most patients were in the 46-55 year age group, as many as 22 patients (22%), while the least were in the 17-25 year age group 2 patients (2%). The distribution based on gender found that male patients had a higher prevalence than female patients, with 56 male patients (56%) and 44 female patients (44%). Sixty-seven patients (67%) had high NLR values, while 33 patients (33%) had normal NLR values. There were 80 patients (80%) who had high CRP values, while patients with normal CRP values were 20 patients (20%).

Table 1. Description of Patients Confirmed COVID-19 at Bunda Margonda General Hospital in 2021

Variable	Total	Persentage (%)
Age (Year)		
17 – 25 year	2	2
26 – 35 year	21	21
36 – 45 year	18	18
46 – 55 year	22	22
56 – 65 year	21	21
>65 year	16	16
Gender		
Men	56	56
Women	44	44
NLR		
Normal (< 3.13)	33	33
High (> 3.13)	67	67
CRP		
Normal (< 0.3 mg/dL)	20	20
High (> 0.3 mg/dL)	80	80

Table 2. Bivariate Correlation Test of NLR and CRP Values in Patients Confirmed COVID-19 at Bunda Margonda General Hospital in 2021

Biomarkers	Median (min-max)	P-value	R
NLR[1]	2.83 (0.38 – 23.50)	0.001	0.318
CRP[1]	25 (0.3 – 424)		

In this study, the average NLR value was 2.83, and the average CRP value was 25. In the correlation test, the NLR and CRP variables were found to have a positive and significant correlation with an R-value of 0.318. The correlation between these two variables is weak but still significant. Thus, NLR can replace CRP as a prognostic test in patients with confirmed COVID-19.

DISCUSSION

In a study conducted at Bunda Margonda General Hospital, based on 100 respondents, it was found that the most confirmed cases of COVID-19 were in the age group 46-55 years, with a total of 22 patients (22%). The results of this study are based on research conducted by Guan, which found that the average age of patients with confirmed COVID-19 is 41-57 years (4). Older people experience a degenerative process, namely a decreased organ function and the body's immune system, making them more vulnerable to COVID-19 (9).

Apart from the age category, it is known that most confirmed cases of COVID-19 at Bunda Margonda General Hospital were male, with a total of 56 patients (56%), compared to female patients, with 44 patients (44%). The results of this study are research conducted by Ramirez that men dominate confirmed cases of COVID-19 and have a higher infection rate compared to women. This gender gap is related to social factors that are carried out, namely smoking habits in men (10–12). This is possible because viral receptor enzymes are found in the male body and are called angiotensin-converting enzyme 2 (ACE2) (13).

ACE2 provides a protective impact in chronic pathologies such as hypertension, cardiovascular diseases, and acute respiratory distress syndrome—comorbidities that raise the likelihood of a worse result in COVID-19 patients. The preventive effect of ACE2 has been proven by studies using mouse models that show more severe lung failure with reduced regulation of ACE2 (14).

Acute respiratory failure is brought on by infection with other COVID variations, such as SARS-CoV, which causes ACE2 to be downregulated by binding viral protein spikes to ACE2. This lowers ACE2 expression in the lungs (7). It is fair to assume that COVID-19 and SARS patients have similar case fatality rates, gender biases in illness susceptibility, and acute respiratory distress syndrome (15).

Furthermore, it is well known that women generally have higher innate and immunological responses than men (16). Because of this, women are more effective in battling unusual and contagious infections. In women, estrogen as the principal female sex hormone, has been reported to play a protective role in SARS by boosting the immune response and reducing SARS-CoV replication directly (17). Estrogens can particularly increase the expression of ACE2, and they can also affect the activity of renin-angiotensin system in the other components (18).

Most NLR values in patients with confirmed COVID-19 at the Bunda Margonda General Hospital increased with 67 patients (67%). The results of this study are research conducted by Liu, namely an increase in NLR values by 50% in patients aged> 50 years (19). An increase in the NLR value can occur because patients with confirmed COVID-19 experience a decrease in the number of lymphocytes and an increase in the number of neutrophils (20). It has been proven in a study conducted by Kaleem that examining the NLR value can be used as a simple prognostic test to predict the morbidity and mortality of COVID-19 cases with the advantages of being cheap, readily available, and providing objective evidence (8). The following study can be done with more research subjects to improve the meaning, and it can be done with higher research methods, namely cohorts. The limitation of this study is the retrieval of data in the form of medical record data that is retrospective so that this study can describe the strength of the relationship between variables but does not describe the cause and effect relationships that occur due to the retrieval of data taken at the same time. Future studies investigating the NLR and CRP levels in patients with confirmed COVID-19 are expected to use this work as a reference or guide. Research pertaining to this study is anticipated to be generated and processed utilizing the most recent references to create data that is more ideal, accurate, and superior.

CONCLUSION

A relationship was found between NLR and CRP in patients with confirmed COVID-19. If the NLR value increases, the CRP value will also increase in COVID-19 patients, with a p-value of 0.001 and coefficient correlation=0.318.

ACKNOWLEDGMENTS

Authors thank to Bunda Margonda General Hospital and Faculty of Medicine and Health Universitas Muhammadiyah Jakarta for their support.

CONFLICT OF INTEREST

Authors declare that do not have a conflict of interest and affiliations that could raise biased statements in the discussion and conclusion sections of the paper.

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