VOL. 41, No. 4, October 2021

p-ISSN 0853-7704
e-ISSN 2620-3162

JURNAL RESPIROLOGI INDONESIA

Majalah Resmi Perhimpunan Dokter Paru Indonesia
Official Journal of The Indonesian Society of Respirology

Akreditasi RISTEKDIKTI
Surat Keputusan Menteri Riset dan Teknologi Nomor: 200/M/KPT/2020 Tanggal 23 Desember 2020, Peringkat 2
Website: http://www.jurnalrespirologi.org

JURNAL
RESPIROLOGI INDONESIA

Majalah Resmi Perhimpunan Dokter Paru Indonesia
Official Journal of The Indonesian Society of Respirology

Editorial Office
PDPI Jl. Cipinang Bunder, No. 19, Cipinang Pulo Gadung
Jakarta Timur 13240 Telp: 02122474845
Email : editor@jurnalrespirologi.org
Website : http://www.jurnalrespirologi.org

Publisher
The Indonesia Society of Respirology (ISR)
Published every 3 months (January, April, July & October)

Jurnal Respirologi Indonesia
2nd Rank Accreditation
According to the Decree of the Minister of Research and Technology/Head of the National Research and Innovation Agency of the Republic of Indonesia Number: 200/M/KPT/2020
December 23, 2020

JURNAL
RESPIROLOGI INDONESIA

Majalah Resmi Perhimpunan Dokter Paru Indonesia
Official Journal of The Indonesian Society of Respirology

VOLUME 41, NUMBER 4, October 2021

TABLE OF CONTENT

Original Article

The Role of Neutrophil-Lymphocyte Ratio (NLR), Platelet-Lymphocyte Ratio (PLR), and D-Dimer in Predicting the Outcome of Confirmed COVID-19 patients

Fathiyah Isbaniah, Tomu Juliani, Triya Damayanti, Dewi Yenita, Faisal Yunus, Budhi Antariksa, Wahyu Aniwidyaningsih, Sita Laksmi Andarini, Diah Handayani

Pulmonology Department and Respiratory Medicine Faculty of Medicine University of Indonesia, Persahabatan Central Hospital, Jakarta

Abstract

Background: *Cytokine storm or hyperinflammation condition in COVID-19 patients could result in fatal outcomes. Inflammation could also result in coagulation disorders. The Neutrophil-Lymphocyte Ratio (NLR) and Platelet-lymphocyte ratio (PLR) have been known as inflammation markers in several diseases. D-dimer value can be used to assess a patient's coagulation status. Further study on thromboinflammation biomarkers in COVID-19 patients is needed. Therefore, we conducted a study to assess the association between NLR, PLR, and d-dimer on the clinical outcome of confirmed COVID-19 patients at Persahabatan Central Hospital.*

Methods*: Observational cohort retrospective analysis was conducted on 214 medical records of confirmed COVID-19 patients who meet the inclusion criteria in Persahabatan Central Hospital from March to July 2020.*

Results*: The mean patient's age in this study is 54.35 years, dominated by male patients (60.7%). Most of the patients had normal nutritional status (54.7%). The proportion of patients with comorbidities is 65.4%. The most common comorbid is hypertension, followed by diabetes mellitus. 76.1% of patients have severe-critically ill disease, followed by moderate (20.1%) and mild disease (3.7%) The length of hospitalization median were 12 days. Sixty patients (28%) have died during hospitalization. The median of initial value of NLR, PLR, and d-dimer is 5.75 (0.68–81.5), 243.5 (44.7–1607), and 1140 (190–141300) respectively. We found significant associations between NLR (P=0.0001), PLR (P=0.013) and d-dimer (P=0.032) on clinical outcome.*

Conclusion*: Initial value of NLR, PLR, and D-dimer of confirmed COVID-19 patients at Persahabatan Central Hospital were associated with clinical outcome.* ***(J Respirol Indones 2021; 41(4): 236–44)***

Keywords: *coronavirus disease 2019; neutrophil lymphocyte ratio; platelet lymphocyte ratio; D-dimer; mortality.*

Hubungan Nilai Rasio Netrofil Limfosit, Rasio Platelet Limfosit dan D-dimer dengan Luaran Tatalaksana Pasien COVID-19 Terkonfirmasi di RSUP Persahabatan

Abstrak

Latar belakang: *Badai sitokin atau kondisi hiperinflamasi pada pasien dengan COVID-19 dapat berakibat fatal pada pasien. Infalmasi dapat menyebabkan gangguan kogulasi. Rasio neutrofil limfosit (RNL) dan rasio platelet limfosit (RPL) telah diketahui dapat menjadi penanda inflamasi pada beberapa penyakit. Status koagulasi asien dapat dilihat dari parameter nilai D-dimer. Peran penandahayati yang dapat menggambarkan keadaan trombоinflamasi pada pasien COVID-19 tersebut perlu ditelaah lebih lanjut.*

Metode: *Analisis observasional kohort retrospektif terhadap pasien COVID-19 terkonfirmasi yang dirawat di RSUP Persahabatan secara total sampling hingga diperoleh 214 rekam medis yang memenuhi kriteria inklusi dari bulan Maret sampai Juli 2020.*

Hasil: *Rerata usia pasien pada penelitian ini adalah 54,35 tahun, didominasi oleh laki-laki sebanyak 60,7%. Status gizi pasien paling banyak adalah normal sebesar 54,7%. Proporsi pasien yang memiliki komorbid sebanyak 65,4%. Komorbid yang paling banyak adalah hipertensi, kedua adalah diabetes melitus. Derajat penyakit paling banyak adalah berat-kritis sebanyak 76,1%, diikuti sedang 20,1%, ringan 3,7%. Median lama rawat adalah 12 hari. Pasien meninggal sebanyak 60 orang (28%). Nilai median RNL, RPL dan D-dimer awal pasien adalah 5,75 (0,68–81,5), 243,5 (44,7–1607) dan 1140 (190–141300), secara berurutan. Terdapat hubungan antara nilai RNL (P=0,000), RPL (P=0,013) dan D-dimer (P=0,032) terhadap luaran pasien.*

Kesimpulan: *Nilai RNL, RPL dan D-dimer awal perawatan pasien COVID-19 terkonfirmasi di RSUP Persahabatan berhubungan dengan luaran tatalaksana pasien.* ***(J Respirol Indones 2021; 41(4): 236–44)***

Kata kunci: *coronavirus disease 2019; rasio netrofil limfosit; rasio platelet limfosit; D-dimer; mortalitas*

Correspondence: Fathiyah Isbaniah
Email: fathiyah21@gmail.com

INTRODUCTION

The world has been facing a global pandemic since late 2019. COVID-19 is a viral infection presumed to originate from animals in an animal market in Wuhan, China.[1] After less than one year, the disease has spread from China to every country. On July 28th 2020, it was documented that 16.341.920 confirmed COVID-19 cases around the world, and 650.805 patients have died from it. In Indonesia, the authors' country, up to 100.303 cases have been confirmed, and up to 4.838 patients have died.[2] This number keeps growing as the infection keeps growing and the number of cases fluctuates.

The aetiology of this disease is severe-acute respiratory syndrome corona virus-2 (SARS-CoV-2).[1] The clinical manifestation of COVID-19 varies from mild symptoms like coughing to life-threatening symptoms leading to respiratory failure, muscular pain, and eventually death.[3,4] The severe manifestations are more commonly found in patients with comorbidities such as hypertension, diabetes mellitus, cardiovascular and cerebrovascular disease.[3]

SARS-CoV-2 infection leads to systemic inflammation, the release of pro-inflammatory cytokines, and migration of pro-inflammatory macrophages and granulocytes into the inflamed tissue, leading to massive tissue destruction.[5] Lymphopenia found in patients with COVID-19 indicates dysregulation of the immune system affecting lymphocytes.[6] This dysregulation also causes platelet numbers changes, as it has been found that platelets also play an essential role as an immune modulator.[7] The combination of systemic inflammation and immune dysregulation results in a hypercoagulable state, leading to increased complications of arterial and venous thromboembolism.[8]

This hyper-inflammation and immunological parameter changes raise a significant issue in patients with confirmed COVID-19 infection. Previous studies have reported neutrophil-lymphocyte-ratio (NLR) and platelet-lymphocyte-ratio (PLR) may be used to evaluate immunological and inflammation status in confirmed patients.[9–12] Coagulation status and its complications can be assessed using D-dimer.[13] However, these studies were primarily based in China, which may differ from other countries. Therefore, the author would like to analyse the association between NLR, PLR, and D-dimer levels to predict and the prognosis of patients with early COVID-19 infection in order to provide a better and more effective treatment.

METHODS

We performed a cohort retrospective clinical study on the clinical manifestation and laboratory results of all patients with confirmed COVID-19 in Persahabatan Central Hospital from October to November 2020 that met the inclusion and exclusion criteria. The patients involved met the inclusion criteria of (1) confirmed COVID-19 cases based on RT-PCR examination; (2) patients had completed hospitalisation from March to June 2020. Patients who met exclusion criteria were excluded. Exclusion criteria were: (1) incomplete required data (2) patients who did not complete hospitalization due to personal reasons; (3) pregnant patients; (4) patients with Human Immunodeficiency Virus (HIV) infection; (5) patients with Dengue Haemorrhagic Fever (DHF) infection; and (6) patients with chronic hepatitis infection.

Data collected includes COVID-19 RT-PCR confirmation, length of hospitalisation, treatment outcome, age, gender, nutritional status, disease severity, comorbidity, haemoglobin level, leukocyte count, thrombocyte, lymphocyte count, albumin, NLR, PLR, and D-dimer level in an early stage of hospitalisation. The data involved originated from the medical records of Persahabatan Central Hospital.

Data extracted from medical records was recorded and filed in an excel database and analysed using SPSS version 20.0 software. We grouped the patients into patients who finished hospitalisation and patients who died during hospitalisation. We compared patients' age, haemoglobin, leukocyte, platelet, neutrophil count, lymphocyte count, albumin, NLR, PLR, and d-dimer between those who finished

the hospitalisation group and patients who died during the hospitalisation group using the unpaired T-test, Mann-Whitney, and Chi-Square tests. Each variable's optimal cut-off values were analysed using receiver operator curve (ROC) analysis with a confidence interval of 95%.

RESULTS

Clinical characteristics and initial laboratory parameters of study subjects are provided in Table 1. Of the 425 subjects of confirmed COVID-19 patients hospitalised at Persahabatan Central Hospital from March to June 2020, 211 subjects were excluded for being pregnant, having HIV, DHF, chronic hepatitis B infection, request to move to another hospital, and incomplete data. Only 214 subjects were included. 130 (60.7%) of the confirmed COVID-19 subjects were male, and the average age was 54.35 years old, with 24 years old as the minimum and 83 years old as the maximum. The majority of patients (54.7%) had normal nutritional status, 4.2% had below-normal nutritional status, and 41.1% had above-normal nutritional status.

Comorbidities were found in 65.4% of total study subjects, with hypertension (33.2%) as the most common comorbidity, followed by Type-2 Diabetes Mellitus (32%), and cardiac disease (12.6%). Other comorbidities, including cerebrovascular disease (CVD), pulmonary tuberculosis, malignancy, vertigo, severe head trauma, and femoral fracture, were also recorded. The length of hospitalisation's median is 12 days, with one day as the minimum and 40 days as the maximum. Sixty patients (28%) died during hospitalisation, while the rest were discharged.

The median of haemoglobin was 13.4 (7.8–17.9), the median of leukocyte was 9,030 (2,450–28,870), the median of platelet was 265,500 (57,000–880,000), the median of neutrophil count was 77.8 (34.4–97.8), the median of lymphocyte count was 13.65 (1.2–54.6). The median of albumin was 3.5 (1.9–4.9), the median of NLR was 5.75 (0.68–81.5), the median of PLR was 243.5 (44.7–1,607), and the median of D-dimer was 1,140 (190–141,3000).

Bivariate analysis of each variable on patients' outcomes is provided in Table 2. The analysis showed a significantly high frequency of deaths during hospitalisation found in patients over 50 years old. The length of hospitalisation's median in patients who died was 7 (1–40) days, which was significantly different from those who finished hospitalisation with a median of 14 (2–37) days (P=0.0001). The leukocyte (P=0.001), neutrophil percentage (P=0.0001), lymphocyte percentage (P=0.0001), albumin (P=0.0001), NLR (P=0.0001), PLR (P=0.013), and D-dimer (P=0.32) were also significantly different among those who died and those who finished hospitalization.

Disease severity was classified as mild, moderate, and severe. Nutritional status was assessed based on the WHO classification of body mass index (BMI). Based on the presence of comorbidities, subjects were grouped into those with no comorbidity, those who had 1 comorbidity, or had >1 comorbidity. We compared the mortality rates of male and female patients and discovered that 36 male patients died compared to 24 female patients, but the difference was not statistically significant. Initial disease severity was related to the patients' outcome (P=0.0001). Patients who were initially presented with severe disease were more likely to die than those with mild and moderate disease. No patients with mild diseases were reported to die.

This study used the receiver operator curve (ROC) to predict treatment outcome based on significant variables, as shown in figure 1 and 2. The figure showed that the area under the curve (AUC) of NLR, PLR, d-dimer, neutrophil, and leukocyte were better compared to albumin, lymphocyte, and length of hospitalisation. Based on AUC analysis from SPSS software, we found that the AUC of NLR was 0.704 (CI 95%: 0.628–0.779); the AUC of PLR was 0.610 (CI 95%: 0.509–0.680); the neutrophil count was 0.725 (CI95%: 0.651–0.798); and the leukocyte count was 0.649 (CI95%: 0.565–0.733). The optimal cut-off value and its respective sensitivity and specificity are provided in Table 4.

Table 1. Clinical Characteristics of Study Subjects

Variable	Frequency	Percentage	Mean
Gender			
Male	130	60.7	
Female	84	39.3	
Age (Year)			54.35 ± 13.55
Nutritional Status			
Malnourished	9	4.2	
Normal	117	54.7	
Pre-obsed	69	32.2	
Grade I Obesity	12	5.6	
Grade II Obesity	6	2.8	
Grade III Obesity	1	0.5	
Presence of comorbidities			
No comorbid	74	34.6	
1 comorbid	91	42.5	
2 comorbid	40	18.7	
3 comorbid	7	3.3	
4 comorbid	2	0.9	
Disease severity			
Mild	8	3.7	
Moderate	43	20.1	
Severe-critically ill	163	76.1	
Clinical outcome			
Finished hospitalization	154	72	
Died during hospitalization	60	28	
Length of hospitalization (day)			12 (1–40)
Types of comorbidities			
Hypertension	71	33.2	
Diabetes Melitus	68	32	
Congestive Heart Failure	14	6.5	
Coronary Artery Disease	12	5.6	
Cerebrovascular Disease	11	5.14	
Tuberculosis	5	2.34	
History of Tuberculosis	5	2,34	
Appendicitis	3	1.4	
Malignancy	3	1.4	
Asthma	2	1	
Arythmia	1	0.5	
COPD	1	0.5	
Severe head trauma	1	0.5	
Femoral fracture	1	0.5	
Obstructive Ileus	1	0.5	
Takayasu arteritis	1	0.5	
Thoracotomy	1	0.5	
Renal transplant	1	0.5	
Vertigo	1	0.5	

Table 2. Comparison of age, length of hospitalization and laboratory parameter on clinical outcome.

Variable	Clinical outcome		*P*
	Finished hospitalization	Died during hospitalization	
Age (Year)			
Mean	52.85 ± 14.22	58.2 ± 10.85	**0.004**[a*]
<50 years old	61 (80.3%)	15 (19.7%)	**0.045** ‡
≥50 years old	93 (67.4%)	45 (32.6%)	
Gender			0.889 ‡
Female	60 (71.4)	24 (28.6)	
Male	94 (72.3)	36 (27.7)	
Disease Severity			**0.0001** ‡
Mild	8(100)	0	
Moderate	42 (97.7)	1 (2.3)	
Severe-critically ill	104 (63.8)	59 (36.2)	
Nutritional Status			0.166 ‡
Malnourished	7 (77.8)	2 (22.2)	
Normal	78 (66.7)	39 (33.3)	
Pre-obese and Obese	69 (78.4)	19 (21.6)	
Presence of Comorbidity			0.258 ‡
No comorbidity	58 (78.4)	16 (21.6)	
1 comorbidity	64 (70.3)	27 (29.7)	
> 1 comorbidity	32 (65.3)	17 (34.7)	
Length of hospitalization (days)	14 (2–37)	7 (1–40)	**0,0001** §
Haemoglobin	13.4 (7.8–16.6)	13.25 (8.9–17.9)	0.796§
Leukocyte	8,670 (2,450–28,870)	10,730 (3,870–24,180)	**0.001**§
Thrombocyte	271,000 (57,000–880,000)	250,500(119,000–564,000)	0.309§
Neutrophil (%)	73.8 (34.4–97.8)	85.1 (53.9–94.1)	**0.0001**[*]
Lymphocyte (%)	15.65 (1.2–54.6)	8.75 (2.7–39.2)	**0.0001**§
Albumin	3.6 (2.1–4.9)	3.4 (1.9–3.9)	**0.0001**§
NLR	4.715 (0.68–81.5)	9.955 (1.38–34.6)	**0.0001**§
PLR	217.2 (44.7-1,607)	275.5 (77–651.6)	**0.013**§
D-dimer	1,055 (190–35,200)	1,185 (260–141,300)	**0.032**§

Note: *M T-Test; ‡ Chi square; § Mann-Whitney

Table 3. Association of length of hospitalization and laboratory parameters

Variable	Association between length of hospitalization (days)			
	Finish hospitalization (n=154)		Died during hospitalization (n=60)	
	Correlation coefficient	*P*	Correlation coefficient	P-value
Age (years)	0.131	0.105[a]	0.063	0.635[*]
Haemoglobin	-0.052	0.525[a]	0.170	0.193[*]
Leukocyte	0.056	0.492[a]	-0.089	0.498[*]
Thrombocyte	0.001	0.994[a]	0.153	0.244[*]
Neutrophl percentage	**0.313**	**0.000[a]**	-0.346	**0.007**[*]
Lymphocyte percentage	**-0.274**	**0.001[a]**	0.285	**0.027**[*]
Albumin	**-0.254**	**0.001[a]**	-0.109	0.406[*]
NLR	**0.269**	**0.001[a]**	-0.288	**0.026**[*]
PLR	**0.226**	**0.005[a]**	-0.142	0.278[*]
D-dimer	-0.012	0.886[a]	-0.011	0.933[*]

Note: *Spearman Correlation

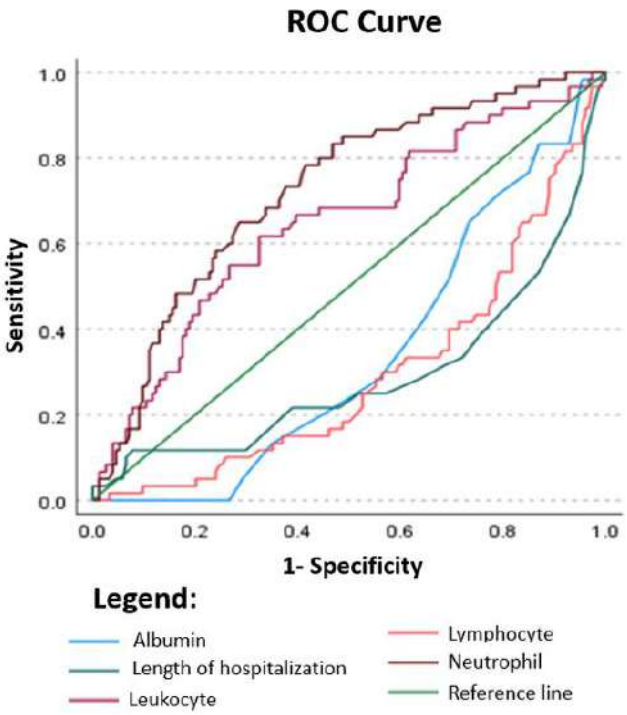

Figure 1. ROC Curve of Albumin, Length of hospitalization, leukocyte, lymphocyte, and neutrophil in predicting clinical outcome. The ROC curve shows how neutrophil and leukocyte count could be used to predict clinical outcome. Cut-off value of each variable are provided in Table 1.

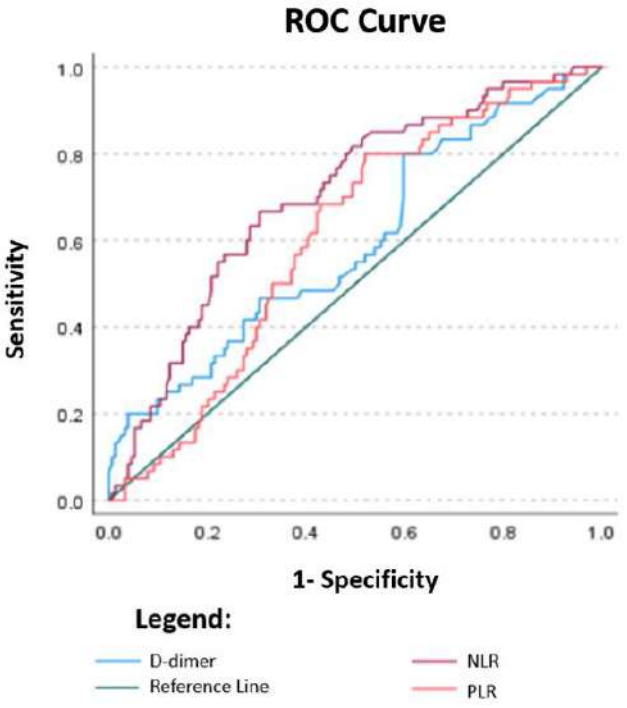

Figure 2. ROC Curve of D-dimer, NLR, and PLR in predicting clinical outcome. ROC curve shows how D-dimer, NLR, and PLR can be used to predict clinical outcome. Cut-off value provided in Table 1.

Table 4. Cut-off value of NLR, PLR, d-dimer, leukocyte, and neutrophil in predicting clinical outcome

Variable	Cut-off Value	Sensitivity	Specificity
NLR	7,035	66,7%	69,5%
PLR	243,5	68,3%	57,1%
D-dimer	1960	46,7%	69,5%
Leukocyte	9595	61,7%	67,5%
Neutrophil	81,95	65%	71,4%

DISCUSSION

It has been more than one year now since the first case of COVID-19 was reported in Wuhan, China.[1] The disease has spread worldwide, causing many deaths and morbidity among all ages. In July 2020, more than 4,500 people died because of this disease in Indonesia, and the number keeps on growing every day.[2] This disease causes systemic inflammation and immune dysregulation, leading to severe tissue destruction and poor outcome.[5] Previous studies performed in China show that several laboratory biomarkers may be used to predict mortality outcomes among patients.[7] However, there was no data from other countries outside of China regarding the result. Therefore, we performed analysis on several laboratory biomarkers on patients' outcomes to evaluate those biomarkers' ability to predict outcomes in the Indonesian population.

Bivariate analysis showed the significant role of age in determining patients' outcome. Like in the previous studies by Zhou et al. and Wu et al.[14,15] We found that the median length of stay of patients who died during hospitalisation was shorter (7 days) than those who finished hospitalisation (14 days). These findings may be explained by the rapid clinical deterioration in that group. This result was like Zhou et al. with a median of 7 days compared to 12 days in those who finished hospitalization.[14]

On laboratory parameters, we found that leukocyte count, neutrophil percentage, lymphocyte percentage are significantly different among the two groups with *P*=0.001, *P*=0.0001, and *P*=0.0001, respectively. We did not find a significant difference in haemoglobin and platelet count between the two groups. A study by Yan et al. also shows similar results, except for the lower platelet value found in patients who died during hospitalisation.[16]

Our study's median of albumin is significantly lower in the group of patients who died during hospitalisation (3.4 [1.9–3.9] compared to patients who finished treatment (3.6 [2.1–4.9] with *P*=0.0001. Several studies have reported similar results by Zhou et al., Yan et al., and Huang et al.[14,16,17] Huang reported that hypoalbuminemia less than 3.5 g/mL could be used as an independent factor to predict death. Albumin is also related to other inflammatory markers such as C-reactive protein (CRP), leukocytes, and NLR. Hypoalbuminemia in COVID-19 may be explained by inflammation-induced capillary permeability elevation leading to albumin shift to the interstitial space.[17] Hypoalbuminemia may also happen because albumin is a negative acute-phase protein that usually decreases during inflammation.[18]

Our study found that the initial value of NLR, PLR, and d-dimer are related to patient outcome with *P*=0.0001; *P*=0.013; and *P*=0.032 respectively. Similar results reported by Yan et al. that report initial high NLR values are related to poor outcomes. The NLR value is an independent risk factor that can be used to predict mortality from all causes during hospitalisation.[16] Qu et al. reported that peak PLR value is an independent factor contributing to disease progression and severe COVID-19 while initial PLR results do not.[19] Zhang et al. reported that an initial d-dimer value above 2,000 g/mL could effectively predict hospital mortality.[20] These results may be explained by the elevation of neutrophil and platelet counts and the decrease in lymphocyte counts.

We discovered no difference in treatment outcome based on gender, nutritional status, or comorbidity. Patients with severe-critically ill disease have significantly higher mortality than moderate and mild disease, similar results as the previous study by Zhou.[14] Our findings differ from Petrilli et al. They reported that BMI >40 was associated with severe disease.[21] They stated that obesity may induce chronic inflammation and increase ACE-2 protein, leading to increased risk of respiratory distress.[22] The lack of an association between nutritional status in our study may be explained as most subjects involved in the study have normal nutritional status.

Bivariate analysis on patients' age, gender, disease severity, and comorbidity presence were not related to the length of hospitalisation. Liu et al. previously reported that age, gender, and comorbidity were not associated with the length of hospitalisation, while disease severity was significantly associated with disease severity. The majority of our subjects were severe to critically ill patients, whereas the majority of Liu's subjects were moderate cases.[23]

In the group of patients who finished hospitalisation, we found a significant relationship between neutrophil, lymphocyte, albumin NLR, and PLR on length of hospitalisation with a low correlation coefficient of 0.313, -0.274, -0.254, 0.269, and 0.226, respectively. While in the group of patients who died during hospitalisation, we found significant relations only between neutrophil, lymphocyte, and NLR on length of hospitalisation with a correlation coefficient of-0.346, 0.285, and 0.288, respectively. Liu et al., previously reported that lymphocyte count was related to length of hospitalisation but not leukocyte, neutrophil, and D-dimer[23], while Yan et al. reported that NLR above 11.75 was related to a longer length of hospitalisation compared to those with NLR below 11.75 (*P*<0.001).[16]

In our study, the applicable cut-off of initial NLR, PLR, D-dimer, leukocyte, and neutrophil count were observed using the ROC curve, giving the results of 7.035, 243.5, 1960, 9595, and 81.95, respectively. However, the cut-off value above has low sensitivity and specificity. Yan et al., who also studied the use of NLR as a prognostic and predictive factor in COVID-19 patients, reported an NLR cut-off value of 11.75 and an AUC of 0.945 (CI 95%: 0.917–0.973) with 97.5% sensitivity and 78.1% specificity. Higher subjects included in the Yan et al. study may explain this difference.[16] Ye et al. also reported a cut-off value for initial NLR of 7.13 with an AUC of 0.86 (CI 95%: 0.73–0.87) with 349 subjects.[24] Zhang et al. reported the optimal cut-off-value of D-dimer to predict in-hospital mortality was 2,000 with an AUC of 0.89, 92.3% sensitivity, and 83.3% sensitivity.[20] We have not found a previous study reporting the cut-off value of PLR to predict mortality in COVID-19 patients.

Several limitations existed in our study. First, our study's design was an observational retrospective on one healthcare centre that highly relies on medical records to gain complete data. Second, most of our subjects are severely-critically ill symptomatic patients. Therefore, our study results may not represent all patients with COVID-19, especially those with mild or asymptomatic infections. In conclusion, initial NLR, PLR, and D-dimer in confirmed COVID-19 patients in Persahabatan Central Hospital are related to treatment outcome. However, further research with more significant subjects may be needed to ensure NLR, PLR, and D-dimer's association with treatment outcome.

CONCLUSION

Initial NLR, PLR, and D-dimer values may predict treatment outcome in confirmed COVID-19 patients.

REFERENCES

1. Handayani D, Hadi DR, Isbaniah F, Burhan E, Agustin H. Penyakit Virus Corona 2019. J Respirol Indones. 2020;40(2):119–29.
2. World Health Organization. Coronavirus disease 2019 (COVID-19) situation report. World Health Organization. 2020.
3. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061–9.
4. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708–20.
5. Tufan A, Avanoğlu Güler A, Matucci-Cerinic M. COVID-19, immune system response, hyperinflammation and repurposing antirheumatic drugs. Turkish J Med Sci. 2020;50(SI-1):620–32.
6. Wang F, Nie J, Wang H, Zhao Q, Xiong Y, Deng L, et al. Characteristics of Peripheral Lymphocyte Subset Alteration in COVID-19 Pneumonia. J Infect Dis. 2020;221(11):1762–9.
7. Jenne CN, Kubes P. Platelets in inflammation and infection. Platelets. 2015;26(4):286–92.
8. Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers DAMPJ, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;191:145–7.
9. de Jager CPC, Wever PC, Gemen EFA, Kusters R, van Gageldonk-Lafeber AB, van der Poll T, et al. The Neutrophil-Lymphocyte Count Ratio in Patients with Community-Acquired Pneumonia. PLoS One. 2012 Oct;7(10).
10. Tamhane UU, Aneja S, Montgomery D, Rogers E-K, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol. 2008;102(6):653–7.
11. Uslu AU, Küçük A, Şahin A, Ugan Y, Yılmaz R, Güngör T, et al. Two new inflammatory markers associated with Disease Activity Score-28 in patients with rheumatoid arthritis: neutrophil-lymphocyte ratio and platelet-lymphocyte ratio. Int J Rheum Dis. 2015;18(7):731–5.
12. Ying H-Q, Deng Q-W, He B-S, Pan Y-Q, Wang F, Sun H-L, et al. The prognostic value of preoperative NLR, d-NLR, PLR and LMR for predicting clinical outcome in surgical colorectal cancer patients. Med Oncol. 2014;31(12):305.
13. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18(4):844–7.
14. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054–62.
15. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med. 2020;180(7):934–43.

16. Yan X, Li F, Wang X, Yan J, Zhu F, Tang S, et al. Neutrophil to lymphocyte ratio as prognostic and predictive factor in patients with coronavirus disease 2019: A retrospective cross-sectional study. J Med Virol. 2020;92(11):2573–81.
17. Huang J, Cheng A, Kumar R, Fang Y, Chen G, Zhu Y, et al. Hypoalbuminemia predicts the outcome of COVID-19 independent of age and co-morbidity. J Med Virol. 2020;92(10):2152–8.
18. Castell J V, Gómez-Lechón MJ, David M, Fabra R, Trullenque R, Heinrich PC. Acute-phase response of human hepatocytes: regulation of acute-phase protein synthesis by interleukin-6. Hepatology. 1990;12(5):1179–86.
19. Qu R, Ling Y, Zhang Y-H-Z, Wei L-Y, Chen X, Li X-M, et al. Platelet-to-lymphocyte ratio is associated with prognosis in patients with coronavirus disease-19. J Med Virol. 2020;92(9):1533–41.
20. Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost. 2020;18(6):1324–9.
21. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: Prospective cohort study. BMJ. 2020;369.
22. Morais AH de A, Aquino J de S, da Silva-Maia JK, Vale SH de L, Maciel BLL, Passos TS. Nutritional status, diet and viral respiratory infections: perspectives for severe acute respiratory syndrome coronavirus 2. Br J Nutr. 2021;125(8):851–62.
23. Liu X, Zhou H, Zhou Y, Wu X, Zhao Y, Lu Y, et al. Risk factors associated with disease severity and length of hospital stay in COVID-19 patients. J Infect. 2020;81(1):e95–7.
24. Ye W, Chen G, Li X, Lan X, Ji C, Hou M, et al. Dynamic changes of D-dimer and neutrophil-lymphocyte count ratio as prognostic biomarkers in COVID-19. Respir Res. 2020;21(1):169.