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D-dimer level differences in pneumonia patients than in COVID-19

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ABSTRACT

Introduction: Pneumonia, also known as pneumonia, is caused by inflammation of the air sacs (alveoli) in one or both lungs. In severe pneumonia, intravascular and intra-alveolar coagulation occurs, which is a response to local and systemic inflammatory processes. The clinical consequence of these changes in coagulation is an increase in the level of D-Dimer which causes death. The purpose of this study was to evaluate D-Dimer in 29 pneumonia patients and 37 COVID-19 patients at Jemursari Hospital.

Methods: This research is quantitative with a cross-sectional analytic observational method. The research sample was obtained from the Jemursari Islamic Hospital in Surabaya for pneumonia and Covid-19 patients in 2021.

Results: The results of the study, a number of women more than men. In women 63,6% and in men 36,4%, while the age is 46-54 years in pneumonia patients 28% and in Covid-19 patients 30%. D-Dimer levels in pneumonia patients 1001-2000 ng/mL were 35% higher compared to COVID-19 patients 501-1000 ng/mL were 30%. Mann Whitney's non-parametric test results obtained p=0.041 (p<0.05), meaning that there was a difference in D-Dimer levels between pneumonia patients and COVID-19.

Conclusion: D-Dimer levels were more elevated in pneumonia patients than in Covid-19, so Covid-19 infection did not exacerbate coagulation and fibrinolysis activities.

Keywords: *COVID-19, Pneumonia, D-Dimer*.
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INTRODUCTION

Pneumonia can be caused by a viral, bacterial, or fungal infection. SARS-CoV-2 is infected with a type of virus that can cause pneumonia. Pneumonia by the COVID-19 virus can cause dangerous complications, one of which is acute respiratory distress syndrome (ARDS). Pneumonia by bacteria, such as Mycobacterium tuberculosis can occur together with other lung diseases.[1]

Pneumonia is one of the leading causes of death in children worldwide. The World Health Organization (WHO) estimates that 15% of deaths in children under 5 years are caused by this disease. The WHO also states that in 2017, more than 800,000 children died of pneumonia.[2] In a study involving 65 men and 37 women, D-dimer levels with a median of 1,550 ng/ml (170 ng/ml -14,690 ng/ml), D-Dimer levels in the multilobar group with a median of 2,060 ng/ml were more[3] compared to the unilobar group (1,230 ng/ml), no correlation was obtained between the two groups (Duarte et al., 2015). High plasma D-dimer levels can predict mortality in pneumonia patients aged 2 to 59 months.[4]

In COVID-19 patients it is estimated that 10-15% will develop a critical form of illness that progresses to severe pneumonia, hypoxia, and respiratory failure, all of which require supportive care and oxygen.[5,6] Of the 113 Covid-19 patients who did not survive, their D-Dimer levels reported an average of 4,600 ng/mL, while the 161 survivors had an average D-Dimer level of 600 ng/mL, higher D-Dimer levels. in COVID-19 patients with pneumonia (p<0.05).[7] Similar results were reported in another study conducted in China between January 1 and February 13, 2020 (Tang et al., 2020) D-Dimer levels in 134 COVID-19 patients who died an average of 4,700 ng/ml, while 315 patients who did not die had an average D-Dimer level of 1,470 ng/ml.[8] According to Durmaz, 2016, D-Dimer levels were high in pneumonia patients.[9] Elevated levels of D-Dimer significantly correlated with the severity of pneumonia also suffered by COVID-19 sufferers.[10]

From some of the results of the research above, it has not been revealed whether D-Dimer levels are the cause of death in Covid-19 patients, in terms of whether D-Dimer levels are higher in COVID-19 patients than pneumonia patients.[11] Therefore, the purpose of this study was to evaluate D-Dimer in 29 pneumonia patients and 37 COVID-19 patients at Jemursari Hospital.

MATERIALS AND METHODS

Materials

Secondary data from the Results of Thorax Photos to determine the diagnosis of pneumonia and Sars-Cov2 RT-PCR results to diagnose Covid-19 with Real-time PCR. D-Dimer levels were carried out using the FIA (Fluorescent Immunoassay) method with the I-Chroma device at the Jemursari Islamic Hospital in 2021.

Data collection procedures

This type of research is quantitative with a cross-sectional analytic observational

method. The research sample was obtained from the Jemursari Islamic Hospital in Surabaya for pneumonia and Covid-19 patients in 2021. The inclusion criteria for both study groups were positive pneumonia results on chest X-rays. In the Covid-19 group, the RT-PCR Covid-19 positive, and in the Pneumonia group, the RT-PCR Covid-19 negative, therefore in this study was divided into two research groups, namely 29 positive pneumonia patients and 37 patients with positive pneumonia and COVID-19.

Data analysis

Secondary data was obtained data on age, sex, and levels of D-Dimer. The three variables were tested for normality by the Shapiro-Wilk test, if the results were normally distributed, the homogeneity test was continued. If both tests are normal and homogeneous, then an independent t-test is performed and if it is not normal and not homogeneous, then the Mann-Whitney test is performed.

RESULTS

Characteristics of Subjects

Table 1 shows that the respondents (55%) were 19-81 years old. The 46- 54year age group was highest in pneumonia patients as much as 28% and in COVID-19 patients as many as 30%. Based on gender, it shows that the male group was 48% of pneumonia patients and 27% of COVID-19 patients and the female group was 51.7% of pneumonia patients and 73% of COVID-19 patients.

Identification distribution of D-Dimer levels in 37 pneumonia patients and 29 COVID-19 patients in Rumah Sakit Jemursari Surabaya. The results of Table 2 showed that the D-Dimer group increased High 1001-2000ng/mL in pneumonia patients by as much as 35% and D-Dimer increased High 500-1000ng/mL in COVID-19 patients by as much as 30%. The distribution of normal D-dimer levels (<500ng/mL) in pneumonia patients was 10% and in COVID-19 patients as much as 24%.

The results of the analysis normality test Shapiro-Wilk of Table 3 showed that was performed on age with P=0,002, sex with P=0,000, and D-Dimer with P=0,000, so it can be concluded that all results were not normally distributed with P=0.000 (P<0.05).

The results of the analysis of Mann Whitney of Table 4 showed test results on the D-Dimer levels with P value = 0.041 (P < 0.05), which means that there is a difference in D-Dimer levels between the two research groups.

Table 1. Distribution of respondents' characteristics in Jemursari Hospital Surabaya

Characteristic	Pneumonia Patients		COVID-19 Patients	
	Total	Percentage (%)	Total	Percentage (%)
Age				
19 – 27 years	1	3	7	19
28 – 36 years	4	14	2	5
37 – 45 years	6	21	3	8
46 – 54 years	8	28	11	30
55 – 63 years	6	21	10	27
64 – 72 years	3	10	2	5
73 – 81 years	1	3	2	5
Sex				
Male	14	48	10	27
Female	15	52	27	73

Table 2. Distribution of D-Dimer levels in 37 patients pneumonia and 29 patients coronavirus in Jemursari Hospital Surabaya

D-Dimer levels	Total	Percentage (%)
Pneumonia Patients		
Normal (<500ng/mL)	3	10
High 500-1000ng/mL	5	17
High 1001-2000ng/mL	10	35
High 2001-4000ng/mL	5	17
High 4001-8000ng/mL	3	10
High 8001-16.000ng/mL	1	3
High >16.000ng/mL	2	6
COVID-19 Patients		
Normal (<500ng/mL)	9	24
High 500-1000ng/mL	11	30
High 1001-2000ng/mL	9	24
High 2001-4000ng/mL	4	11
High 4001-8000ng/mL	0	0
High 8001-16.000ng/mL	2	5
High >16.000ng/mL	2	5

Table 3. Analysis normality test Shapiro-Wilk of age, gender, and D-dimer levels in 29 pneumonia patients and 37 COVID-19 patients in Jemursari Hospital Surabaya

Variables	Statistic	df	P value
Age	0.933	66	0.002
Sex	0.609	66	0.000
Group	0.631	66	0.000
D-Dimer	0.884	66	0.000

Table 4. Analysis Mann Whitney of the two research groups

Variables	Statistics	P value
D-Dimer	382.000	0.041

DISCUSSION

The results of this study indicate that D-dimer levels in COVID-19 patients caused by viruses, not bacteria, provide lower D-dimer levels than patients with pneumonia caused by bacteria. The results of this study are not the same as the

results of Bilian Yu, 2020 which stated that D-dimer levels were significantly increased in COVID-19 patients compared to community-acquired pneumonia (CAP) patients with P<0.05.[12]

Endothelial cell dysfunction caused by infection leads to excessive thrombin formation and cessation of fibrinolysis, suggesting a hypercoagulable state in patients with infection. In addition, hypoxia that occurs in severe pneumonia can stimulate thrombosis not only through increased blood viscosity but also through hypoxia-induced transcription factor-dependent signaling pathways. Therefore, coagulopathy can be found in many patients with severe pneumonia.[12]

However, if D-dimer levels were associated with inflammatory markers, especially from the hsCRP results (R = 0.426, P < 0.05), and low Spearman correlation test results between VTE (venous thromboembolism) scores and D-dimer levels (R Spearman = 0.264, P > 0.05), these results attenuate the role of D-dimer in the prediction of thrombosis.[12] The average result of increased D-dimer levels in CAP patients is higher than in COVID-19 patients, so it can be concluded that D-dimer levels in predicting thrombosis cannot be used as a cause of death in COVID-19 patients.[7]

Plasma D-dimer levels are directly related to intra and extravascular coagulation that occur due to acute and chronic lung damage in community-acquired pneumonia (CAP) patients with an average plasma D-dimer level of 776.1 ± 473.5 ng/mL in patients with comorbidities and 494.2 ± 280.1 ng/mL and patients without comorbidities (p<0.05).[2] These results are similar to those of Ozlem Güneysel's 2008 study which produced patients with non-severe CAP and severe CAP, both of which showed significantly increased plasma D-dimer levels (p=0.04) compared to the median and range of 600 ng/ml. (100-5100 ng/ml). The plasma D-dimer cut-off point > 400 ng/ml as a predictor of mortality in pneumonia patients gave a sensitivity of 73.3% (95% CI; 44.9–92.0) and a specificity of 70.0% (95% CI; 50, 6- 85.2) and accuracy of 71.1%, compared to the control group (p<0.05, p<0.001).[13]

In Covid-19 patients, inflammatory cells are generated during a cytokine release storm. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) driven in part by interleukin-6[14] can cause damage to elastic fibers in the lungs by the formation of bullae. The development of pulmonary fibrosis is likely due to diffuse alveolar destruction with cellular fibro myxoid exudate, desquamation of pneumocytes, and hyaline membrane formation characteristic of Acute Respiratory Distress Syndrome (ARDS).[15] This is similar to the findings seen in post-mortem lung biopsy pathology reports of the SARS and Middle East Respiratory Syndrome coronaviruses. CT findings, in this case, showed areas of advanced fibrosis with bullae formation. Peak levels of D-Dimer and CRP did not show any association with outcome, even though all received anticoagulation therapy. Research suggests that SARS-CoV-2 can cause profound early vascular compromise resulting in a ventilation-perfusion mismatch with the resulting hypoxemia.[16]

The weakness of this study is that it has not detected the role of high D-Dimer early in infection in the pneumonia group compared to low (normal) D-Dimer levels at the start of infection in Covid-19 patients for the incidence of death. So the role of D-Dimer as a cause of death is unknown. The advantage of this study is that the D-Dimer examination in Covid-19 patients is not needed, because most are normal.

CONCLUSION

D-dimer levels with levels < 2000 ng/ml were most commonly found in patients with pneumonia caused by bacteria, these levels were higher than D-dimer levels in COVID-19 patients (<1000 ng/ml) with p = 0.041 (p < 0.05), so it can be concluded that D-dimer levels cannot be associated with a poor prognosis in COVID-19 patients, because levels of less than 500 ng/ml are still more common as much as 24.3% in COVID-19 patients. Furthermore, it is necessary to investigate whether more cases die at high D-Dimer levels of 500-2000 ng/mL in pneumonia patients than at relatively low D-Dimer levels of 500-1000 ng/mL in COVID-19 patients.

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CONFLICT OF INTEREST

There isn't any conflict of interest to declare.

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None.

AUTHOR CONTRIBUTION

All authors contributed to this research starting from the sampling, data collection, and analysis stages, as well as the preparation of articles, and submitting, as well as article revisions.

ETHICAL CONSIDERATION

This research was approved by the Health Research Ethics Committee of Universitas Nahdlatul Ulama Surabaya. Letter of exemption Ref. No. 083/KEPK-RSISJS/VII/2022

REFERENCES

1. Demelo-Rodríguez P, Cervilla-Muñoz E, Ordieres-Ortega L, Parra-Virto A, Toledano-Macías M, Toledo-Samaniego N, et al. Incidence of asymptomatic deep vein thrombosis in patients with COVID-19 pneumonia and elevated D-dimer levels. Thromb Res. 2020;192.
2. Arslan S, Ugurlu S, Bulut G, Akkurt I. The association between plasma d-dimer levels and community-acquired pneumonia. Clinics. 2010;65(6).
3. World Health Organization. WHO | Pneumonia. Who. 2016.
4. Saraswati R, Hakim DDL, Garna H. Kadar D-Dimer Plasma sebagai Prediktor Kematian Penderita Pneumonia Usia 2–59 Bulan. Majalah Kedokteran Bandung. 2012;44(1).
5. Kurniawati D, Prasetyo B, Pandu H, Nurdianto AR. Clinical presentation of maternal death with COVID-19 in rural tertiary care center: A retrospective-descriptive Study. Bali Medical Journal. 2022;11(1):87–90.
6. Minanti BR, Soelistijo SA, Pranoto A. Characteristic profiles of patients with diabetes mellitus and COVID-19 during the second epidemic wave in East Java, Indonesia: a retrospective study. Bali Medical Journal. 2023;12(1):1120–6. Available from: www.balimedicaljournal.org
7. Yu B, Li X, Chen J, Ouyang M, Zhang H, Zhao X, et al. Evaluation of variation in D-dimer levels

among COVID-19 and bacterial pneumonia: a retrospective analysis. J Thromb Thrombolysis. 2020;50(3).
8. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. Journal of Thrombosis and Haemostasis. 2020;18(4).
9. Durmaz N, Selçuk Duru N, Elevli M, Çivilibal M, Şahin K. Evaluation of Serum D-dimer Levels in Children with Pneumonia. Haseki Tıp Bülteni. 2016;54(1).
10. Gungor B, Atici A, Baycan OF, Alici G, Ozturk F, Tugrul S, et al. Elevated D-dimer levels on admission are associated with severity and increased risk of mortality in COVID-19: A systematic review and meta-analysis. Vol. 39, American Journal of Emergency Medicine. 2021.
11. Rahman S, Yusuf M, Rizal S, Amirsyah M, Pratama R. Risk assessment for surgeries during covid-19 pandemic in dr. Zainoel abidin hospital, banda aceh, indonesia. Bali Medical Journal. 2021;10(1):387–91.
12. Yu HH, Qin C, Chen M, Wang W, Tian DS. D-dimer level is associated with the severity of COVID-19. Thromb Res. 2020;195.
13. Güneysel O, Pirmit S, Karakurt S. Plasma d-dimer levels increase with the severity of community acquired pneumonia. Tuberk Toraks. 2004;52(4).
14. Zhang C, Wu Z, Li JW, Zhao H, Wang GQ. Cytokine release syndrome in severe COVID-19: interleukin-6 receptor antagonist tocilizumab may be the key to reduce mortality. Int J Antimicrob Agents. 2020;55(5).
15. Marini JJ, Gattinoni L. Management of COVID-19 Respiratory Distress. Vol. 323, JAMA - Journal of the American Medical Association. 2020.
16. George B, Megally M, Mrejen-Shakin K. SPONTANEOUS PNEUMOTHORAX AND SPONTANEOUS PNEUMOMEDIASTINUM IN NON-INTUBATED PATIENTS IN THE SETTING OF SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2. Chest. 2020;158(4).