



D-DIMER AS A PROGNOSIS OF THE SEVERITY OF COVID-19 PATIENTS AT BEKASI REGENCY HOSPITAL

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Abstrak

Peningkatan D-dimer digunakan untuk menilai tingkatan risiko dan ketahanan hidup pasien Covid-19 dan dapat menjadi penanda prognosis yang buruk. Tujuan penelitian ini untuk melihat rata-rata kadar D-dimer yang signifikan pada pasien terkonfirmasi Covid-19 dengan derajat keparahan. Metode yang digunakan adalah Penelitian Retrospektif dengan teknik purposive sampling berdasarkan kriteria derajat keparahan penyakit Covid-19. Data pasien diambil dari rekam medis dan kadar D-dimer dari Sistem Informasi Laboratorium kemudian dianalisis menggunakan uji Anova satu arah. Hasil menunjukkan rata-rata kadar D-dimer sebesar 2,66 mg/L pada derajat kritis, 2,02 mg/L pada derajat berat, 0,30 pada derajat sedang dan 0,26 pada derajat ringan. Pasien laki-laki menempati prosentase lebih besar daripada pasien perempuan dengan jumlah 62,5%. Usia 46-65 tahun menduduki prosentase terbanyak sebesar 55% untuk kategori abnormal disebabkan oleh sistem imun sebagai pelindung tubuh tidak bekerja sekuat ketika masih muda. Penelitian ini menunjukkan adanya perbedaan rata-rata signifikan pada kelompok derajat keparahan ringan dengan berat, ringan dengan kritis, sedang dengan berat, dan sedang dengan kritis. Untuk peneliti selanjutnya diharapkan dapat menganalisis parameter pemeriksaan hemostasis yang lain dengan variabel derajat keparahan penyakit.

Kata kunci: Coronavirus, COVID-19, D-dimer, parameter koagulasi, pembekuan darah

Abstract

The increase in D-dimer is the most significant change in coagulation parameters in Covid-19 patients and can be a marker of poor prognosis. The purpose of this study was to see the average significant D-dimer levels in patients with confirmed Covid-19 with severity. The method used is Retrospective Research with a purposive sampling technique based on the criteria of the severity of Covid-19 disease. Patient data was taken from medical records and D-dimer levels from the Laboratory Information System and then analyzed using a one-way Anova test. The results showed an average D-dimer level of 2.66 mg/L at critical degrees, 2.02 mg/L at severe degrees, 0.30 at moderate degrees and 0.26 at mild degrees. Male patients occupy a larger percentage than female patients with a total of 62.5%. The age of 46-65 years occupies the highest percentage of 55% for the abnormal category because the immune system as a protector of the body does not work as strongly as when it was young. This study showed a significant average difference in the groups of mild severity with severe, mild with critical, moderate with severe, and moderate with critical. For the next researcher, it is expected to be able to analyze other hemostasis examination parameters with variables of disease severity.

Keywords: Coronavirus, COVID-19, D-dimer, coagulation parameters, blood clotting

1. INTRODUCTION

D-dimer is a degradation product of fibrin formed during the breakdown of blood clots by fibrinolysis. An increase in D-dimer in the blood is a marker of thrombosis. Elevated D-dimer levels are found in deep vein thrombosis, pulmonary embolism, arterial thrombosis, disseminated intravascular coagulation (DIC), pregnancy, inflammation, cancer, chronic liver disease, trauma, surgery, and vasculitis. Frequent increase in D-dimer found in severe Covid-19 patients and is predictor occurrence of ARDS, need care in the care unit intensive, and death (Willim, Hardigaloe and Supit, 2020). Positive examination results show that thrombus is present, but can't show the location of abnormalities and get rid of other potential etiologies (Widjaja, 2010).

Increased D-dimer is the most significant change in coagulation parameters in severe Covid-19 patients and occurs more frequently than other coagulation parameters such as prothrombin time (PT) or A PTT. In addition, coagulation parameters showed a marked tendency towards thrombosis, as changes in other parameters indicating a bleeding tendency, such as very low platelets or fibrinogen levels, were absent. Progressively increasing values can be used as a prognostic parameter indicating a worse outcome.

D-dimer level, factor prognostic important was found to be higher in patients with clinically severe cases of SARS-CoV-2 than in less severe cases. Better understanding of factors This prognostic can help doctors predict severity of illness and need for nursing unit care intensive care unit (ICU) in patients infected with SARS-CoV-2. This meta-analysis aims to determine association of D-dimer with disease severity and mortality in SARS-CoV-2 patients.

Studies show that enhancement D-dimer levels can be marker of poor prognosis in patients with coronavirus disease (Covid-19). Pandemic period, stratification risk in triage required, and D-dimer may be one indicator potential in the patient's case risky tall. However, the mere presence of high D-dimer is not a sufficient reason to start giving anticoagulant therapeutic (Nugroho, 2020).

2. RESEARCH METHOD

This research was carried out at Record Medical and Laboratory Regional public hospital Bekasi Regency Jl. Raya Teuku Umar No. 202, Wanasari, District. Cibitung, Bekasi, West Java 17520 in June 2021 by knowing D-dimer levels with various level degrees severity (mild, moderate, severe and critical) in Covid-19 sufferers who do maintenance intensive in space isolation of Bekasi Regency Hospital in the period January – March 2021.

2.1 Design study

This research is a descriptive research analytical with a *Cross Sectional approach*, the data is processed statistically using the One-way *Anova* test which aims to analyze the variance contained in the variable tied to all groups carried out comparison. If the Anova test results show that H_0 fails to be rejected (there is no difference), then the Post Hoc Test is not carried out. However, if the test results show that H_0 is rejected (there is a difference), then a further test (Post Hoc Test) must be carried out to find out which variables have significant differences.

2.2 Research data collection

Collecting data on patients who tested positive for COVID-19 d-dimer levels during the period January – March 2021 includes name, gender, age, clinical diagnosis patient,

Select patient data that meets condition criteria inclusion along with degrees its severity as many as 10 sample data per each category, if requirements have been stated appropriate, next record d-dimer examination result data, summarize the examination result data obtained then the data is processed and presented in tabular form.

2.3 Data Presentation

Data obtained analyzed with descriptive statistics and inferential statistics, with the help of the program. Data analysis was carried out in two ways, namely: univariate analysis and analysis bivariate.

Analysis The bivariate used is *One Way ANOVA*. If there is difference, then followed by a *Post Hoc test* to find out variable which has it significant difference. If assumptions homogeneity variance not met, one technique that can be used are *Games-Howell*.

2.4 Research Ethics

This research has been approved by the Bekasi Regency Hospital with No.

3. RESULTS AND DISCUSSION

3.1 Results Univariate Data Distribution Frequency

Table 1. Frequency Distribution of d-dimer Examination Results with different degrees of severity

Mark	Degrees Critical	Degrees Heavy	Medium Degree	Degrees light
Average (mg/L)	2.66	2.02	0.30	0.26
Minimum	1.10	0.60	0.10	0.05
Maximum	3.70	4.00	0.40	0.50
Standard Deviation (SD)	0.90	1.24	0.10	0.26

800/3980/RSUD/2021 with permission from the National Unity and Political Agency of the Bekasi Regency Regional Government Number: 070/570/Kesbangpol/2021. The researcher guarantees that this research will be carried out in accordance with the applicable standard operating procedures (SOP) so that it can minimize risks and not harm any party. The researcher promised to maintain the confidentiality of data obtained from disinterested parties. The information obtained will only be used for research purposes.

Table 1. Distribution Frequency of d-dimer examination results with degrees different severity value 2.66 mg/L in deg critical, 2.02 mg/L at degree weight, 0.30 in degrees medium and 0.26 in degrees light. Minimum value 1.10 mg/L in deg critical, 0.60 mg/L at

degree weight, 0.10 mg/L in degree moderate, and 0.05 mg/L at degree light. Maximum value of 3.70 mg/L at deg critical, 4.00 mg/L at degree weight, 0.40 mg/L in degree moderate, and 0.50 mg/L at degree light.

3.1.2 Examination of d-dimer with differences type sex

Table 2. Distribution Frequency of d-dimer examination results with differences type sex

D-dimer levels	Man		Woman		Total	
	Σ	%	Σ	%	Σ	%
Normal	13	32.5	7	17.5	20	50 %
Abnormal	12	30 %	8	20 %	20	50 %

Table 2 shows distribution frequency of D-dimer examination results with differences type sex from a total of 40 patients obtained normal levels in men of 13 patients with a percentage 32.5 %, women of 7 patients with a percentage of 17.5%. For

abnormal levels in men of 12 patients with a percentage by 30% and in women as many as 8 patients with percentage 20%. In conclusion, more men were confirmed as having Covid -19, amounting to 62.5%.

3.1.3 D-dimer examination based on age

Table 3. Distribution Frequency Grouping of D-dimer levels based on age

Group Patient Age (Years)	d-Dimer group				Total patients based on group age
	NORMAL		ABNORMAL		
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)	
12-25	1	5 %	0	0 %	1
26-45	9	45 %	5	25 %	14
46-65	10	50 %	11	55 %	21
>65	0	0 %	4	20 %	4
Total	20	100%	20	100%	40

Table 3 shows group aged 12 – 25 years there was 1 patient in the normal category with a percentage amounted to 5%, aged 26 – 45 years there were 9 patients with a percentage amounting to 45% for the normal category, aged 46 – 65 years there were 10 patients with a percentage by 50%. Abnormal levels aged 12 – 25 years were 0 patients in the normal category with a percentage amounted to 0%, aged 26 – 45 years there were 5 patients with a percentage amounting to 25% for the normal category, aged 46 – 65 years there were 11 patients with a percentage amounting to 55%, and age > 65 years as many as 4 patients with a percentage of 20%.

3.1.4 One Way Anova Test Results

One-Way ANOVA is used to analyze the variance among groups by comparing their means. This method is most accurate when each group has the same sample size. It involves one dependent variable and one independent variable. If the ANOVA test results show H_0 fails to be rejected (no difference), then further testing (Post-Hoc Test) was not carried out. However, if the test results show that H_0 is rejected (exists differences), then further tests (Post-Hoc Tests) must be carried out to find out, variables which one has it? Significant difference.

Table 4. *One Way Anova Test Results*

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	44,492	3	14,831	24,765	,000
Within Groups	21,559	36	,599		
Total	66,051	39			

Table 4 displays Sig .000. which means it can be concluded that “ There is Difference in average D-dimer levels in COVID-19 patients by degree The severity in the Bekasi District Hospital is significant.

3.1.5 Multiple Comparison Games-Howell Post Hoc Test Results

The Games-Howell post-hoc test is another nonparametric approach to

comparing combinations of groups or treatments. The Post hoc *Games-Howell test* is somewhat similar to the Tukey test in its formulation, the *Games-Howell test* does not assume equal variances and sample sizes. The *Games-Howell test* was performed on the ranking variables similar to other nonparametric tests. Because the Games-Howell test does not rely on equal variances and sample sizes, it is often recommended over other approaches such as the Tukey test.

Table 5. Multiple Comparison Games-Howell Post Hoc Test

(I) Group degrees severity	(J) Group degrees severity	Mean Difference (IJ)	Std. Error	Sig.	95 % Confidence Interval	
					Lower Bound	Upper Bound
LIGHT	CURRENTLY	-.04000	.06137	,913	-.2163	1,363
	HEAVY	-1.76000 *	.39602	,007	-2.9880	-.5320
	CRITICAL	-2.40000*	.29027	,000	-3.2950	-1.5050
CURRENTLY	LIGHT	.04000	.06137	,913	-.1363	.2163
	HEAVY	-1.72000 *	.39407	,008	-2.9467	-.4933
	CRITICAL	-2.36000 *	.28760	,000	-3.2530	-1.4670
HEAVY	LIGHT	1.76000 *	.39602	,007	.5320	2.9880
	CURRENTLY	1.72000 *	.39407	,008	.4933	2.9467
	CRITICAL	-.64000	.48557	,565	-2.0251	.7451
CRITICAL	LIGHT	2.40000 *	.29027	,000	1.5050	3.2950
	CURRENTLY	2.36000 *	.28760	,000	1.4670	3.2530
	HEAVY	.64000	.48557	,565	-.7451	2.0251

*. The mean difference is significant at the 0.05 level.

Table 5 show that group showing exists group mean differences degrees severity (marked with a sign star “ * ”) and a Sig value < 0.05 is degrees severity light with heavy, light with critical, medium with heavy, and moderate with critical.

3.2 Discussion

Laboratory parameters that can be used to identify happen disturbance Blood coagulation in Covid-19 patients is D-dimer, fibrin/fibrinogen, *prothrombin time* (PT: time required for blood to form clots/ platelets) or

can be expressed in INR (International Normalized Ratio: standardization international for PT measurement results). Study of 94 patients in China, Han et al (2020) reported that D-dimer value, product fibrin/fibrinogen (*fibrin degradation product*, FDP) and fibrinogen (FIB) degradation in all SARS-CoV-2 cases was substantially higher compared with healthy controls. D-dimer and FDP levels in patients with severe SARSCoV-2 infection turns out to be higher compared to patients with milder infections when compared with healthy

controls, prothrombin time activity was lower in SARS-CoV-2 patients.

A number of conditions with increased D-dimer Venous thrombosis, DIC, infarction myocardial, inflammation, sepsis, cancer, pregnancy, postoperative, trauma, burns, bleeding, stroke, age more, syndrome nephrotic, liver cirrhosis. In this study, patients with VTE (*venous thromboembolism*) were included in the category factor exclusion. VTE is the most common disease very occurs and can have an impact Serious Because covers second condition abnormality blood clots i.e. *deep vein thrombosis* (DVT) and *pulmonary embolism* (PE). D-dimer examination is an accepted examination panel wide as inspection screening initial stage of treatment patient suspect VTE, D-dimer can also be used as inspection support addition besides radiology for criteria go home patient take care hospitalization with VTE. However, D-dimer has limited specificity.

Based on the severity of the case, COVID-19 is divided into several groups: asymptomatic, mild, moderate, severe, and critical. However, in this study, the researchers did not include D-dimer levels for asymptomatic cases because the research setting only admitted patients categorized as mild, moderate, severe, and critical. Patients confirmed to have asymptomatic COVID-19 are recommended to undergo self-isolation and strictly follow health protocols.

Based on age obtained group age namely 46-65 years occupy percentage the most by 50% for the normal category ; and 55% for the abnormal category. The same statement was also made by (Nareza, 2020) that as it increases age, body will experience various decline due to the aging process, starting from decreasing hair color pigment

production, production hormones, elasticity skin, mass muscle, density bones, strength teeth, up to function of body organs. Study similar was also carried out by , the results of the research also found as many as 35.7% were elderly own sufficient attitude and as many as 23.5 % have sufficient attitude towards prevention transmission of Covid-19 in groups carry on. Age a person can influence the knowledge he has, will but at age carry on ability to receive and remember something knowledge provided will reduced, so if elderly own lacking knowledge so will impact on behavior carried out in prevention transmission of Covid-19 in groups age carry on.

Research result found There is a number of elderly still not completely apply protocol health, where it was found that elderly families did not wear masks when accompanying them elderly, then also discovered elderly get together with neighbors around the house without using a mask. Apart from that, it was also found elderly who never carry hand sanitizer when leaving the house, do it exercise only sometimes and do not do inspection health independent at home because they don't have medical equipment so that elderly come to service health to do inspection. However This research is not in line with research (Al-Hanawi *et al.*, 2020) who stated that Older adults tend to have better knowledge and practice, than younger people.

System immune as protector the body doesn't work as strong when still young. This is it reason why do people continue age (elderly) is vulnerable attacked various diseases, including Covid-19 which is caused by the Corona virus. Compiled by health articles , not a little elderly people who have chronic diseases, such as heart , diabetes. This could improve risk or danger

coronavirus infection. Complications that arise the consequences of Covid-19 will also be more severe when The sufferer already has these diseases. Not just cause lung disorders, Corona virus infection can also reduce function of body organs others, so existing chronic disease conditions sufferer will the more serious, even resulting in death. This research also supports it facts that have been circulating for a long time If Ages 12-25 years are less likely to be exposed to Covid-19 because occupy percentage of 5% of amount population (recorded number 19 of 375). Health Journal created by (Sari, Yaslina and Suryati, 2020) state that student own knowledge of the Covid-19 virus by category tall. In this case the teacher plays a role active in giving big contribution to students to give knowledge the danger of the Covid-19 virus, the teacher succeeded give his knowledge to student as well as student capable understand it well According to research (Khusairi, 2020) role students in overcoming Covid-19 through formation Sat group volunteers are also categorized as "good". The role of students is very much needed to participate contribute to dealing with Covid-19 by partnering Covid-19 volunteers, they are on their own offer self become volunteers to help public. Teenager own speed, toughness, intelligence, as well network to initiate innovation based technology so that makes it easier public even taker decisions or policies in their respective regions and they can play a role in reducing spread and increase in cases of this corona virus.

There is difference in average D-dimer levels in Covid-19 patients by degree Severity. This is in line with research conducted by (Aditia *et al.*, 2020) that D-dimer levels can be consideration in giving thromboprophylaxis and can be a strategy One way to judge the occurrence of the coagulation process in Covid-19 patients by

carrying out D-dimer examination. Enhancement D-dimer levels illustrate Activation from system moderate coagulation and fibrinolysis taking place. In Covid-19 patients, the majority experience enhancement D-dimer levels 2 – 3 times that normal value. Initial research in China reports an increase in D-dimer > 0.5 mcg/ml occurred in 46% of patients, as well there is signs Activation factor coagulation like thrombocytopenia mild and prolongation of prothrombin time. Fei Zhou et al, in their research states, patients with D-dimer levels > 1.0 mcg/ml have risk 18 times more deaths.

4. CONCLUSIONS AND SUGGESTIONS

4.1 Conclusions

Based on the research conducted, it can be concluded that more men (62.5%) are confirmed positive for COVID-19. Patients aged 46-65 years have the highest percentage, with 50% in the normal category and 55% in the abnormal category. There are significant differences in the average D-dimer levels among COVID-19 patients with varying severity levels in Bekasi District Hospital, particularly between mild to severe, mild to critical, moderate to severe, and moderate to critical cases.

4.2 Suggestions

Further research on the analysis of other hemostasis examination parameters, including platelet count, *prothrombin time* (PT), *activated partial thromboplastin time* (APTT), *thrombin time* (TT), factor VIII plasma fibrinogen with variable degree disease severity.

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