JIKW

pISSN 1978-2071 | eISSN 2580-5967
Jurnal Ilmiah Kedokteran Wijaya Kusuma 13(1): 25-37, March 2024

ARTICLE INFO

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Article history
Received 03-08-2023
Revised 05-01-2024
Accepted 22-03-2024
Available online

Please cite this article in APA 7th Style:
Arimbi M. R., Indrajanu I. N., Hernanda P. Y. (2024). D-Dimer As A Parameter Of Disease And Death Of Covid-19 Patients In Islamic Hospital, Surabaya. *Jurnal Ilmiah Kedokteran Wijaya Kusuma*, 13(1), pp. XX-XXX https://doi.org/10.30742/jikw.v13i1.3194

D-Dimer as A Parameter of Disease and Death of Covid-19 Patients in Islamic Hospital, Surabaya

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Abstract

Background: Previous studies of Community Associated Pneumonia (CAP) and Chronic Obstructive Pulmonary Disease (COPD), patients have shown that D-Dimer increases higher in severe cases and can be used as a prognostic biomarker and whilst D-Dimer> 1 mcg/ ml tends to be death for hospitalized adult patient with a diagnosis of Covid-19. However, D-Dimer's role in Covid-19 patients has not been fully studied. We aim to conduct research on D-Dimer as a parameter of Clinical Severity and Death of Covid-19 Patients in Islamic Hospital, in Surabaya. **Methods:** This type of research is an analytic observational study with a retrospective approach. The population in this study were all patient's data retrieved from the Dahlia Room's database from June to July 2020 which were taken through EMR (an Electrical Medical Records) from a total of 189 patients with the total sample of 82 patients. Data analysis in this study used chi-square (X2) with a significant value of p <0.05. **Results:** Age over 60 years is associated with a higher risk of severe Covid-19 infection (P<0.05). A history of hypertension significantly affects the severity of Covid-19 infection (P < 0.05). The proportion of recoveries (53.7%) was higher than the number of deaths (46.3%), although the majority of patients experienced severe clinical severity (39%). Laboratory parameters, such as D-dimer values, correlated significantly with patient age (P = 0.027, <0.05). **Conclusion:** The study highlights the importance of factors such as age and history of comorbid diseases in predicting the severity of Covid-19 infection. A better understanding of these risk factors can help in more effective management and management of Covid-19 patients.

Keywords: COVID-19, d-dimer, parameters

Original Research Article

INTRODUCTION

The year of 2020 was a tough year for the world when suddenly the Covid-19 outbreak appeared, which initially appeared locally in Wuhan - China, then broke out and ravaged the whole world. Global data as of October 30, 2020 showed that there were 45,018,354 cases with 1,181,027 deaths. Meanwhile, Indonesian data as of October 29, 2020 showed that there were 404,048 cases spread across 34 positive provinces of Covid-19 with 13,701 death. Covid-19 began to emerge at the end of 2019, It began to spread and explode locally in China until the end of January 2020, then spread

throughout the world throughout February to the end of October, with no a single thing tank and strategic thinker in the world, either government private sector, universities,or the World Bank and IMF) take it into account (Alqahtani et al., 2022).

Subsequent research has shown a close relationship with the corona virus which causes Severe Acute Respiratory Syndrome (SARS) that plagued Hong Kong in 2003, until WHO named it the novel corona virus (nCov-19). Not long after, reports began to appear from other provinces in China and even outside of China. People with travel history from the cities of Wuhan and China, namely South Korea, Japan, Thailand, the United States, Macau, Hong Kong, Singapore, Malaysia, up to a total of 25 countries. including France, Germany, United Arab Emirates, Vietnam and Cambodia. The threat of the pandemic is getting bigger when various cases of human-to-human transmission such as doctors and medical personnel who treat patients without any history of traveling to closed markets (Linlin et al., 2020).

Coronavirus 2 (SARS-2) is a severe acute respiratory syndrome that can stimulate pro-thrombotic changes. If this is, combined with endothelial tropism and lung structure, may explain its association with thrombotic events, reduced pulmonary gas exchange, acute respiratory distress syndrome (ARDS) and composite endpoints (intensive care units, invasive ventilation and death). Reported coagulopathy and increased D-Dimer were seen in 3.75 - 68% of covid-19 patients. Previous studies of Community Associated Pneumonia (CAP) and Chronic Obstructive Pulmonary Disease (COPD) patients have shown that D-Dimer increases higher in severe cases and can be used as a prognostic biomarker whilst D-Dimer> 1 mcg / ml tend to be a risk of death. hospitalized adult patient with a diagnosis of Covid-19. However, D-Dimer's role in Covid-19 patients has not been fully studied. Based on this background, we are interested in conducting research on D-Dimer as a Parameter of Clinical Severity and Death of Covid-19 Patients at the Surabaya Islamic Hospital (Zhan et al., 2021).

METHODS

Types of research

This type of research is an analytic observational study with a retrospective approach.

Research population and sample

The eligibility criteria for participants in this study include patients recorded from the Dahlia Room database at Surabaya Islamic Hospital during the period June to July 2020. The participant selection process is carried out through the use of EMR (Electronic Medical Record) which serves as the main data source. Of the total 189 documented patients, only 82 patients were selected as study samples based on certain criteria that may have been previously established. These eligibility criteria include factors such as age, gender, disease history, symptoms, Clinical Severity and Cure Rate.

Data analysis

From the study, the data used were electronic medical data (EMR) from patients recorded in the Dahlia Room database at Surabaya Islamic Hospital during the period June to July 2020. The data includes information on the patient's demographic characteristics, disease history, laboratory parameters, clinical severity, and treatment outcomes. This data was used to analyze factors related to Covid-19 infection, including research on coagulopathy prevalence, disease severity, and other risk factors, while analytically done with two tests, namely the comparison test with the Wilcoxon Rank Sum Test and the correlation test nkapa, or Chi Square with the SPSS program version 26.0 presented as a percentage.

RESULTS

Univariate Analysis

Based on Table 1, it is known that the covid-19 patients in this study with more than 60 years old, as many as 42 people (51.2%) while the other 40 people (48.8%) were patients <60 years old.

Table 1. Distribution of Research Data Based on Age of Covid-19 Patients at the Surabaya Islamic Hospital

Age	Frequency	Percentage%
> 60 years	42	51.2
<60 years	40	48.8
Total	82	100.0

Source: Survey Results, 2020

Based on Table 2, it is known that most of the Covid-19 patients in this study were male, with a total of 45 people (54.9%), female patients were 37 in total number (45.1%).

Table 2. Distribution Based Research Data Gender of Covid-19 Patients at Surabaya Islamic Hospital

Gender	Frequency	Percentage%
Male	45	54.9
Women	37	45.1
Total	82	100.0

Source: Data processed, 2020

Based on Table 3, it shows that the Covid-19 patients in this study who had a history of diabetes mellitus and those who did not have a history of diabetes mellitus were the same, namely 41 people (50%) respectively.

Table 3. Distribution Based Research Data Diabetes Mellitus suffered by Covid-19 patients in Surabaya Islamic Hospital

Diabetes Mellitus	Frequency	Percentage%
Yes	41	50.0
Not	41	50.0
Total	82	100.0

Source: Data processed, 2020

Based on Table 4, it shows that most of the Covid-19 patients in this study did not have a history of hypertension, namely 57 people (69.5%) while 25 people (30.5%) had a history of hypertension.

Table 4. Distribution of Research Data Based on Disease Hypertension suffered by Covid-19 patients in Surabaya Islamic Hospital

Hypertension	Frequency	Percentage%
Yes	25	30.5
Not	57	69.5
Total	82	100.0

Source: Data processed, 2020

Based on Table 5, it shows that most of the Covid-19 patients in this study did not have congenital CKD (Chronic Kidney Disease), with a total number of 75 people (91.5%) while 7 people (8.5%) were claimed to have congenital CKD (Chronic Kidney Disease).

Table 5. Distribution of Research Data Based on Disease CKD (Chronic Kidney Disease) suffered by Covid-19 Patients in Surabaya Islamic Hospital

CKD disease	Frequency	Percentage%
Yes	7	8.5
Not	75	91.5
Total	82	100.0

Source: Data processed, 2020

Based on Table 6, it shows that all Covid-19 patients (100%) in this study did not have congenital bronchial asthma.

Table 6. Distribution of Research Data Based on Disease Bronchial Asthma Affected by Covid-19 Patients in Surabaya Islamic Hospital

Bronchial Asthma Disease	Frequency	Percentage%
Not	82	100.0
Total	82	100.0

Source: Data processed, 2020

Based on Table 7, it shows that most of the respondents in this study did not have a history of coronary heart disease (CHD), with a total number of 79 people (96.3%) while 3 other people (3.7%) were claimed to have a history of coronary heart disease (CHD).

Table 7. Distribution of Research Data Based on Disease Coronary Heart (CHD) suffered by Covid-19 Patients in Surabaya Islamic Hospital

PJK	Frequency	Percentage%
Yes	3	3.7
Not	79	96.3
Total	82	100.0

Source: Data processed, 2020

Based on Table 8, it shows that most Covid-19 patients in this study did not have a history of Stroke, namely 81 people (98.8%), and only 1 person (1.2%) had a history of stroke disease.

Table 8. Distribution of Research Data Based on Disease Stroke suffered by Covid-19 patients in Surabaya Islamic Hospital

Stroke	Frequency	Percentage%
Yes	1	1.2
Not	81	98.8
Total	82	100.0

Source: Data processed, 2020

Based on Table 9, it is known that the results of chest radiographs in Covid-19 patients who show bilateral pneumonia and those without bilateral pneumonia are the same, namely 41 people (50%) respectively.

Table 9. Distribution of Research Data Based on Thorax Photos in Covid-19 Patients at Surabaya Islamic Hospital

Thorax Photo	Frequency	Percentage%
Bilateral pneumonia	41	50.0
Not bilateral pneumonia	41	50.0
Total	82	100.0

Source: Data processed, 2020

Based on Table 10, it shows that most of the clinical severity suffered by Covid-19 patients in this study was classified as severe, namely 32 people (39%) while Covid-19 patients with mild clinical severity were 28 people (34.1%) while Covid patients -19 with moderate clinical severity amounted to 22 people (26.8%).

Table 10. Distribution of Research Data Based on Clinical Severity Covid-19 patient at Surabaya Islamic Hospital

Clinical Severity	Frequency	Percentage%
Light	28	34.1
Moderate	22	26.8
Weight	32	39.0
Total	82	100.0

Source: Data processed, 2020

Based on Table 11, it shows that the proportion of the total cure rate for Covid-19 patients in this study was bigger , namely 44 people (53.7%),than the number of deaths was 38 people (46.3%).

Table 11. Distribution of Research Data Based on Patient Mortality Rate Covid-19 at Surabaya Islamic Hospital

Death Rate	Frequency	Percentage%
Died	38	46.3
Healed	44	53.7
Total	82	100.0

Source: Data processed, 2020

Based on Table 12, it is known that the results of the chi square test showed a significant relationship between the age of Covid-19 patients and the D-Dimer value at Islamic Hospital Surabaya (p = 0.027). There was also a significant association between history of diabetes mellitus (p = 0.013), CKD (p = 0.023), bronchial asthma (p = 0.000), clinical severity (p = 0.002), and patient mortality (p = 0.000) with D-Dimer value measurements. However, there was no significant relationship between gender, hypertension, CHD, stroke, and chest photos with D-Dimer value measurements at Islamic Hospital Surabaya.

Table 12. Relationship of Disease Severity and Death of Covid-19 Patients to the measurement of the d-Dimer value at the Islamic Hospital in Surabaya

No.	Characteristics	*p-value*
1	Age	0.027
2	Gender	0.616
3	Diabetes mellitus	0.013
4	Hypertension	0.134
5	CKD (Chronic Kidney Disease)	0.023
6	Bronchial Asthma	0,000
7	CHD (Chronic Heart Disease)	0.804
8	Stroke	0.409
9	Thorax Photo	0.260
10	Clinical Severity	0.002
11	Patient Death	0,000

Source: Data processed, 2020

DISCUSSION

Data on the death rate due to COVID-19 is increasing. Previous reports had shown that certain laboratory parameters were related to with disease severity and mortality in SARS-CoV-2 infection. The level of D-Dimer an important prognostic factor, was found to be higher in patients with clinically severe SARS-CoV-2 cases than in non-severe cases. A better understanding of these prognostic factors can help clinicians predict disease severity and the need for intensive care unit (ICU) care in patients infected with SARS-CoV-2. (Nugroho, et.al., 2020)

According to (Long et al., 2020), D-dimer examination can be used as a new indicator in determining the clinical classification of COVID-19. D-dimer testing is recommended for COVID-19 disease with D-dimer = 2.0 ng / ml allowing for optimal cut-off in prediction of COVID-19 mortality in hospital and D-dimer value.≥ 2.0 ng / ml has a higher risk of death than D-dimer value <2.0 ng / ml. The D-dimer value can be used as a prediction for the prognosis value of mortality in COVID-19 patients (Simadibrata & Lubis, 2020)

This study used 82 data on patients with confirmed COVID-19 with the rapid molecular testing method GeneXpert SARS-CoV-2 (rt-PCR) who had checked the D-dimer value in the Dahlia Room from June to July 2020 at the Islamic Hospital in Surabaya. In addiction the 82 D-dimer results showed that the D-dimer value ≥ 2.0 ng / ml. So that the researchers divided into 2 categories, namely high D-dimer values and normal D-dimer values, this was only to make it easier for researchers to analyze D-dimer values as a parameter viewed from various variables that were suspected to be a factor in the death of COVID-19 patients in Surabaya Islamic Hospital. This study focused on the research variables on ages, gender , and comorbid diseases that patients have including: Diabetes Mellitus (DM), Hypertension (HT), Chronic kidney disease (CKD), Bronchial Asthma (ASBRO), Coronary Heart Disease (CHD), Stroke, Thorax and Clinical Severity and Patient Mortality.

D-dimer value parameter in terms of patient age

In this study, it was known that the majority of respondents as many as 42 people (51.2%) were> 60 years old (Table 5.1). From this prevalence figure, it could be assumed that the majority of respondents in this study were elderly. This is in line with a statement put forward by a doctor who stated that the older person's, the immune system as a body protector does not work as well as when he was young. This was the reason why the elderly were susceptible to various diseases, including COVID-19 which is caused by the Corona virus (Zhang et al., 2022).

Meanwhile, in terms of the D-dimer value parameter for the age variable in this study, it was known that the majority of respondents had a D-dimer value in the High category. This can be clarified from the data obtained (Annex SPSS output). Which from 100% of respondents aged <60 years, it is known that 52.5% of respondents have a D-dimer value in the normal category, while the other from 100% of respondents aged> 60 years, it is known that 71.4% of respondents have a D-dimer value in the high category. This result is reinforced by the acquisition of the chi-square test in this study with a sig = 0.027 (<0.05), which means that a high D-dimer value for the patient's age variable can be an indicator of death / severity of COVID-19 patients at Surabaya Islamic Hospital (Table 5.12).

The increase in the D-dimer value as a parameter in terms of the age variable in this study is in line with research conducted by (Widjaja, 2010) which states that there is an increase in D-dimer levels in older subjects due to the decreased elasticity of blood vessels in older subjects. The loss of elasticity of blood vessels coupled with blood lipid deposits and degenerative processes in old age will cause hemorheological disorders, platelet activation and coagulation factors which can increase the process of thrombus formation. This can lead to death in a person (Lichtman, et.al., 2007)

D-dimer value parameter in terms of gender of the patient

In this study, it is known that the majority of respondents as many as 45 people (54.9%) were male (Table 5.2). This is in line with research data released by the BBC which states that one of the most prominent differences that have emerged regarding COVID-19 is gender. The difference is the mortality rate for men and women. In the US, it is known that twice as many men have died from the virus than women. Likewise in Europe, it is known that 69% of all deaths from the corona virus occur in men. Similar patterns have been seen in China and elsewhere (Bwire, 2020).

While in terms of the D-dimer value parameter for the gender variable in this study, it was known that the majority of respondents have a D-dimer value in the High category. This could be clarified from the data obtained (Annex SPSS output). Where from 100% of male respondents, it is known that 62.2% of respondents have a D-dimer value in the high category, while from 100% of female

respondents, it was known that 56.8% of respondents also have a D-dimer value in the high category. This showed that the D-dimer value of COVID-19 patients who were male or female has the same D-dimer value, which is in the high category. This was reinforced by the results of the chi-square test which obtained a sig = 0.616

The absence of differences in the increase in the D-dimer value as a parameter for the gender variable in this study is in line with the research conducted by (Widjaja, 2010) which states that there was a difference in D-dimer levels in men and women, but it was not statistically significant. Gender does not affect D-dimer levels in the detection of thromboembolic events (Vj et al., 2007).

D-dimer value parameter in terms of patient comorbidities, namely Diabetes Mellitus (DM)

In this study the patients were known to be comorbid diabetes mellitus with patients without comorbid diabetes mellitus amounted to the same, namely 41 people (50%) (Table 5.3). This shows that 50% of the COVID-19 patients in this study had comorbid diabetes mellitus. This result is collaborating data reported by PERKENI which states that Diabetes Mellitus (DM) is a risk factor for increasing the severity of COVID-19 infection. This is also reinforced by data from the Chinese CDC, (2020) which shows the percentage of the death rate for people with diabetes diagnosed with COVID-19 in China at 7.3%. Whereas in Italy, 36% of deaths among COVID-19 patients were related to diabetes (Onder, et.al., 2020).

In this study when viewed from the parameter D-dimer value for the comorbid variable of patients with Diabetes Mellitus (DM), it is known that the majority of respondents with DM comorbid values have D-dimer values in the High category. This could be clarified from the data obtained (Annex SPSS output). Where from 100% of respondents with comorbid DM, it is known that 73.2% of respondents have a D-dimer value in the high category, while from 100% of respondents without DM comorbid, it is known, that 53.7% of respondents have a D-dimer value in the normal category. This is reinforced by the results of the chi-square test which obtained a sig = 0.013 (<0.05), which means that a high D-dimer value for DM comorbid can be an indicator of death / severity of COVID-19 patients at the Surabaya Islamic Hospital (Table 5.12).

Diabetes Mellitus is closely related to thrombosis. Because diabetes mellitus will be accompanied by a prothrombotic state, namely changes in the thrombosis and fibrinolysis processes. This disorder is due to insulin resistance, especially in patients with Type 2 diabetes. Increased fibrinogen and factor VII activity and Plasminogen Activator Inhibitor (PAI-1) in plasma will cause a decrease in urokinase and increase platelet aggregation. Overexpression of PAI-1 is thought to occur due to the direct influence of insulin and proinsulin. Various studies conducted on diabetes mellitus sufferers have reported increased levels of various blood clotting factors that play a role in the intrinsic pathway (kallikrein, vWF, F VIII, FIX, F.XII), as well as those that play a role in the extrinsic pathway (TF and F.VII) (Xiao et al., 2023).

D-dimer value parameter in terms of patient comorbidities, namely Hypertension (HT)

In this study it was known that the majority of patients in this study did not have comorbid hypertension (HT). namely as many as 57 people (69.5%) (Table 5.4). This was in contrast to research data obtained by Chang in China which states that hypertension is one of the comorbidities found in sufferers of COVID-19, around 15% of cases of hypertension are found in COVID-19 patients (Chan et al., 2020).

Moreover in this study, when viewed from the parameter D-dimer value for the comorbid variable of patients with hypertension (HT), it was known that the majority of respondents with comorbid HT have D-dimer values in the High category. This can be clarified from the data obtained (Annex SPSS output). Where from 100% of respondents with comorbid HT, it is known that 72% of respondents have a D-dimer value in the high category, while from 100% of respondents without HT comorbid, it is known that 54.4% of respondents also have a D-dimer value in the high category. This shows that the D-dimer value of COVID-19 patients with comorbid or without comorbid HT has the

same D-dimer value in the high category. This is reinforced by the results of the chi-square test which obtained a sig = 0.134

The absence of differences in the increase in the D-dimer value as a parameter for the hypertension variable in this study strengthened the study conducted by Gunawan which stated that patients with comorbid hypertension were still given hypertension drugs. The use of anti-hypertension drugs such as the ACE inhibitor and ABR drug classes is still recommended for hypertensive patients because there is no clear evidence that these drugs can aggravate COVID19 patients (Gunawan et al., 2020).

D-dimer value parameter in terms of patient comorbidities, namely Chronic Kidney Disease (CKD)

In this study it was found that the majority of patients in this study did not have comorbid Chronic kidney disease (CKD) as many as 75 people (91.5%) (Table 5.5). This is in contrast to data reported by the Indonesian Nephrology Association (PERNEFRI) which stated that kidney failure is known to have a high risk of contracting COVID-19. This was conveyed by dr. Pringgodigdo Nugroho, Sp.PD-KGH who is a member of the Indonesian Nephrology Association (PERNEFRI). If corona occurs in patients with kidney failure, the risk of death will be higher than normal people who are affected by corona (Hidayangsih et al., 2023).

And in this study, if viewed from the parameter D-dimer value for the comorbid variable of patients with Chronic Kidney Disease (CKD), it is known that the majority of respondents with comorbid chronic kidney disease (CKD) have a D-dimer value in the High category. This could be clarified from the data obtained (Annex SPSS output). Where from 100% of respondents with comorbid Chronic Kidney Disease (CKD), it was known that 100% of respondents have a high D-dimer value. This was reinforced by the results of the chi-square test which obtained a sig = 0.023 (<0.05), which means that the D-dimer value for the comorbid variable Chronic Kidney Disease (CKD) is an indicator of death / severity of COVID-19 patients at Surabaya Islamic Hospital. (Table 5.12).

The increase in the D-dimer value in terms of comorbid Chronic kidney disease (CKD) in this study was in line with the theory that virus was reported to stimulate endothelial cells to activate the fibrinolysis process which causes an increase in D-dimer (Orsi et al., 2013).

D-dimer value parameter in terms of patient comorbidities, namely Bronchial Asthma (ASBRO)

From the research data, it was known that all respondents as many as 82 patients (100%) did not have comorbid Bronchial Asthma (ASBRO) (Table 5.6). This was in line with the theory which states that there are no studies that link a history of asthma with the possibility of being infected with SARS-CoV-2 (Susilo et al., 2020).

Meanwhile, when viewed from the D-dimer value parameter for the Bronchial Asthma (ASBRO) variable in this study, it was known that the majority of respondents had a D-dimer value in the High category. This could be clarified from the data obtained (Annex SPSS output). Where from 100% of respondents, it is known that 59.8% of respondents have a D-dimer value in the high category. This is also reinforced by the acquisition of the chi-square test results with a sig = 0.000 (<0.05), which means that the D-dimer value for the comorbid variable Bronchial Asthma (ASBRO) is an indicator of death / severity of COVID-19 patients at the Surabaya Islamic Hospital (Table 5.12).

This result strengthens the statement (Chen et al., 2020) who reported that D-dimer> 1µ g / ml represents a risk of death. According to studies, the meta-analysis conducted by (Yang et al., 2020) showed that COVID-19 patients with a history of respiratory system diseases would tend to have more severe clinical manifestations. The same result is also shown by Yao, who found a significant correlation between D-dimer level and disease severity, were grouped based on lung area affected on chest CT, oxygenation index, and clinical stage according to interim guidelines. In addition, the percentage of outcome elevation in patients with COVID-19 (Yao et al., 2020).

D-dimer value parameter in terms of patient comorbidities, namely Coronary Heart Disease (CHD)

In this study, it was known that the majority of patients in this study did not have comorbid Coronary Heart Disease (CHD) namely as many as 79 people (96.3%) (Table 5.7). This was different from statement from (Alqahtani et al., 2022), which is the heartology division of Brawijaya Saharjo Hospital, which states that besides attacking the lungs, COVID-19 can also make blood thick easily. So, patients who already had heart problems, especially coronary heart problems (CHD), will experience complaints or have the same manifestations as people who have a heart attack because the blood is thick. Heart health and its relation to COVID-19 are related to the tendency to clot blood vessels in Corona patients. These blood clots will increase the risk of heart problems, so that patients who already have a history of the disease will be more susceptible to worsening and dying. (reported bywww.health.detik.com, 2020).

However, when viewed from the parameter D-dimer value for the comorbid variable of patients with coronary heart disease (CHD), it was known that the majority of respondents with comorbid Coronary Heart Disease (CHD) had a D-dimer value in the high category. This could be clarified from the data obtained (Annex SPSS output). Where from 100% of respondents with comorbid Coronary Heart Disease (CHD), it was known that 66.7% of respondents have a D-dimer value in the high category, while from 100% of respondents without comorbid Coronary Heart Disease (CHD),It is known, 59.5% of respondents also have a D-dimer value in the high category. This shows that the D-dimer value of COVID-19 patients with comorbid or non-comorbid Coronary Heart Disease (CHD), both have high category D-dimer values. This was reinforced by the results of the chi-square test which obtained a sig = 0.804 (> 0.05), which means that the D-dimer value for the Coronary Heart Disease (CHD) comorbid variable, was not an indicator of death / severity of COVID-19 patients in hospital. Islam Surabaya (Table 5.12).

An increase in the D-dimer value in terms of comorbid coronary heart disease (CHD), in this study in was line with the research of (Chen et al., 2020) which showed that CHD factors were risk factors for death. This may be because of the percentage of respondents with comorbid CHD in the study was higher than other seriously ill / critically ill cases referred to the hospital, which is another evidence of the correlation between D-dimer levels and CHD (Yao et al., 2020).

D-dimer value parameter in terms of patient comorbidities, namely Stroke

In this study it was found that the majority of patients in this study did not have comorbid stroke as many as 81 people (98.8%) (Table 5.8). This was different from the results of Kurnianto's research which showed that COVID-19 could worsen the condition of stroke patients, this was because stroke and COVID-19 are associated with coagulopathy, anti-phospholipid antibodies, and vasculitis. Clinical manifestations, investigations, and treatment in cases of stroke with COVID-19 need special attention. Handling of stroke with COVID-19 focuses on patient safety and the health safety of health workers (Retnaningsih et al., 2020).

In this study, when viewed from the parameter D-dimer value for the comorbid variable of patients with stroke, it was known that the majority of respondents with comorbid stroke have a D-dimer value in the high category. This could be clarified from the data obtained (Annex SPSS output). Where from 100% of respondents with comorbid stroke, it is known that all respondents have a D-dimer value in the high category, while from 100% of respondents without comorbid stroke, it is known that 59.3% of respondents also have a D-dimer value in the high category. This showed that the D-dimer value of COVID-19 patients with comorbid or non-comorbid stroke has the same D-dimer value, which was in the high category. This was reinforced by the results of the chi-square test which obtained a sig = 0.409

The absence of differences in the increase in D-dimer value as a parameter for the stroke variable in this study strengthens the study (Sharifi et al., 2021) who also conducted a case study of 3 COVID-19 patients with acute ischemic stroke. And from the results of this study, it was found that the three patients also had cardiovascular risk factors such as hypertension, diabetes, and ischemic heart

disease. So it can be said that stroke is not a single factor as an indicator of the severity/ death of COVID-19 patients (Retnaningsih et al., 2020).

The parameter value of D-dimer in terms of comorbid thorax results patient

In this study, it was known that patients with thorax results Bilateral pneumonia with non-bilateral pneumonia patients was the same, namely 41 people (50%) (Table 5.9). And if it was viewed from the parameter D-dimer value for the comorbid variable of patient's thorax results, it was known that the majority of respondents' thorax results have D-dimer values in the High category. This can be clarified from the data obtained (Annex SPSS output). Where from 100% of respondents with bilateral thorax pneumonia results, it was known that 65.9% of respondents have a D-dimer value in the high category, while from 100% of respondents who were not bilateral pneumonia, it is known, 53.7% of respondents also have a D-dimer value in the category. high. This shows that the D-dimer value of COVID-19 patients with bilateral thorax pneumonia results or not bilateral pneumonia has the same D-dimer value, which was n the high category.

There is no difference in the increase in the D-dimer value as a parameter for the variable thorax results in this study contrary to the statement of (Dai et al., 2018) in previous studies that have shown that D-dimer levels are associated with the severity of community-acquired pneumonia and clinical outcomes (Yao et al., 2020).

Meanwhile, the chi-square test results obtained a sig = 0.260 (> 0.05), which means that the D-dimer value for the thorax result variable is not an indicator of death / severity of COVID-19 patients at the Surabaya Islamic Hospital (Table 5.12). It's in line with (Guo et al., 2020) which states that D-dimers have not been used as biomarkers for viral pneumonia. Although D-dimer elevation has been observed in articles describing the clinical features of COVID-19, whether D-dimer level is a marker of severity has not been examined (Yao et al., 2020).

The parameter of the D-dimer value in terms of clinical severity of the patient

In this study, it is known that the majority of patients in this study have clinical severity in the severe category as many as 32 people (39%) (Table 5.10). This classification is enforced according to the guidelines in the book Novel Coronavirus Pneumonia Diagnosis and Treatment Guideline (6th edition) by the National Health Commission of China which divides clinically, the severity of COVID-19 patients is classified into mild, moderate, severe, and critically ill (Qiu et al., 2020).

If it was viewed from the parameter D-dimer value for the patient clinical severity variable, it is known that from 100% of respondents with mild clinical severity, it was known that 64.3% have a normal D-dimer value, while from 100% of respondents with moderate clinical severity, it is known 59.1% had a high D-dimer value. Likewise, from 100% of respondents with severe clinical severity, it was found that 81.2% had high D-dimer values as well. (SPSS output appendix). This shows that the D-dimer value of COVID-19 patients with moderate and severe clinical severity had the same D-dimer value, which was in the high category. This is reinforced by the results of the chi-square test which obtained the sig = 0.002 (<0,05)

This result is in line with the results of research conducted by (Yao et al., 2020) which states D-dimer levels are usually elevated in patients infected with SARS-CoV-2. Significantly higher rates are found in those with critical illness and can be used as a prognostic marker for hospital mortality.

D-dimer value parameter in terms of patient mortality

In this study, it was known that from 82 respondents, the majority had recovered from COVID-19, as many as 44 people (53.7%) (Table 5.11) This strengthens the research results (Liu et al., 2020) who stated that the improvement of eosinophils in patients with low eosinophils was thought to be a predictor of cure. Viewer from the parameter D-dimer value for the patient mortality variable, it was known that from 100% of the respondents who died, it was known that 84.2% had a high D-dimer value, while the other 61.4% had a D-dimer normal value. This shows that the D-dimer value of COVID-

19 patients could be a parameter for the mortality rate and also the cure for COVID-19 patients. This was reinforced by the results of the chi-square test which obtained a value of sig = 0.000 (<0.05), which means that the D-dimer value can be a parameter for the mortality and recovery rates for COVID-19 patients at the Surabaya Islamic Hospital (Table 5.12).

According to (Ramanathan et al., 2020) the prognosis of COVID-19 was influenced by many factors. In the study, it was reported that the mortality rate for severe COVID-19 patients reached 38% with a median length of stay in the ICU to death of 7 days. The rapid increase in cases can overwhelm hospitals with a high patient burden. This increases the mortality rate at the facility (Ji et al., 2020).

Meanwhile, patients who were declared cured do not rule out reinfection (reinfection). Although this was still controversial. Animal studies suggested recovered monkeys cannot catch COVID-19, but there reports that find patients came back positive for rRT-PCR within 5-13 days after being negative twice in a row and being discharged from the hospital. This may be due to reinfection or false negative results on rRT-PCR on discharge (Lan et, al., 2020).

Other researchers also reported the detection of SARS-CoV-2 in the faces of patients who were already negative based on oropharyngeal swabs (Ling et al., 2020). It should be noted that these findings only analyzed the association between D-dimer levels and disease severity and mortality only. There was still insufficient evidence regarding the causative mechanism and whether the link was a specific effect of SARS-CoV-2 infection or a consequence of a systemic inflammatory response (Yao et al., 2020). Although it provides important insights, the study has limitations, such as difficulties in generalizing results and constraints in controlling for confounding factors as well as a small sample size

Add limitation

CONCLUSION

The results of the chi-square test at Islamic Hospital Surabaya showed the relationship between age, diabetes mellitus, CKD, bronchial asthma, clinical severity, and patient mortality with D-dimer value measurements in Covid-19 patients. However, there was no significant association with gender, hypertension, CHD, stroke, or thoracic imaging results.

ACKNOWLEDGEMENTS

The authors declared that there is no conflict of interest.

CONFLICT OF INTEREST

No Acknowledgements

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