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Original Article

EVALUATION OF BMI RELATIONSHIP WITH INCREASED D-DIMER IN COVID-19 PATIENTS AT A JAKARTA PRIVATE HOSPITAL

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ABSTRACT

Objective: Evaluate BMI against increased D-Dimer in Covid-19 patients at one of the private hospitals in Jakarta.

Methods: This study is a retrospective cohort study, and this study only covers COVID-19 patients admitted to a private hospital in the Plumpang area, North Jakarta, Indonesia, from January until July 2021.

Results: The correlation between BMI and D-Dimer of COVID-19 patients using the Mann-Whitney method showed that only ten patients had higher D-Dimer 500 ng/ml, and most patients had lower D-Dimer 500 ng/ml (90%). The survival analysis for COVID-19 patients using the Kaplan Meier method showed that patients receiving normal BMI had an average survival rate of around 64% after about 17 d of treatment.

Conclusion: There is the correlation between BMI with D-Dimer of COVID-19 patients.

Keywords: COVID-19, BMI, D-Dimer, Survival analysis

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INTRODUCTION

Coronavirus 2019 (COVID-19), an emerging respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has recently become a pandemic [1]. Most patients with COVID-19 show mild to moderate symptoms, but about 15% develop severe Pneumonia, and about 5% eventually develop acute respiratory distress syndrome (ARDS), septic shock, and/or multiple organ failure [1]. Although some coronaviruses are ubiquitous among humans and cause only mild illness, the newly emerged coronavirus epidemic was previously observed in SARS in 2002 and Middle East Respiratory Syndrome (MERS) in 2012. And the unprecedented rate of COVID-19 spread has created a critical global health emergency, and the academic community has raced to respond through research development [2].

D-dimers are fibrin formation and degradation biomarkers that can be measured in whole blood or plasma. Healthy individuals have low circulating levels of D-dimers, while high levels are found in conditions associated with thrombosis [3]. The use of proprietary antibodies that recognize different epitopes with various kinetics makes the development of universal references to calibration and standardization impossible [3]. There are two definitions such as a D-dimer unit: a fibrin equivalent unit (FEU); it connects the mass of the D-dimer with the mass of fibrinogen; and D-dimer units (DDU) associated with the D-dimer mass alone. The calibration used for the FEU test compares the mass of the D-dimer with the associated molecular weight of 340 plasma d-dimer levels. In contrast, the DDU test calibration compares the D-dimer's mass with 195 plasma d-dimer levels. Therefore, testing samples for D-dimers with FEU and DDU tests will cause a 1.75-fold difference in the results. In addition, different test manufacturers use unit size (e. g. ng/ml, mcg/ml, etc.) [4].

Body Mass Index is a metric currently used to define the characteristics of height/weight anthropometry in adults and to classify (categorize) them into groups. A common interpretation is that it is an index of individual obesity. It is also widely used as a risk factor for the development or prevalence of some health problems [5]. In collaboration with the International Dietary Energy Consultative Group (IDECG), WPT Professors James, A Ferro-Luzzi, and JC Waterlow, FAO began examining the corresponding BMI cut points at the lower end of the spectrum and the associated functional and health consequences of low BMI [6]. After two working group meetings, conclusions were presented in a publication detailing three classes of Chronic Energy Deficiency (CED):<16.0 BMI = CED grade III; 16.0-16.9 BMI = CED, class II and 17.0-18.4 BMI = CED, class I. A BMI of 18.5 and above but less than 25.0 is considered normal. However, in presenting the final classification of the system, the authors combined three CED values with energy expenditure levels above and below 1.4 Levels of Physical Activity (PAL) × Basal Metabolic Rate (BMR) [6].

MATERIALS AND METHODS

Study design and setting

The research was carried out at a private hospital in Jakarta, Indonesia. The study used a retrospective cohort design included 200 COVID-19 patients. All COVID-19 patients who got BMI and D-Dimer were included in the study. Patients having comorbid cancer, SLE, and pregnant patients were excluded from the study.

Ethical approval

Ethical approval was sourced from the ethical medical committee from the Faculty of Health in Indonesia, and an approval letter, NO: 03/KEPK-UTA45JKT/EC/EXE/11/2021, was given before data collection.

Data collecting and handling

Based on fig. 1, ethical approval was required before conducting this study. The researcher would define the patients by the list of patients in the ward. Before taking the medical record data, the researcher would explain the research and its purpose to the patients with the staff's help. The informed consent was signed as an agreement of the study from the patients. The data were arranged according to socio-demography status and D-Dimer and transferred to clinical research form (CRF). Data were analyzed descriptively by Chi-Square, Fisher, Mann-Whitney, and Kaplan Meier test using SPSS 22 version software. Significance correlation was shown by P-value<0.05.

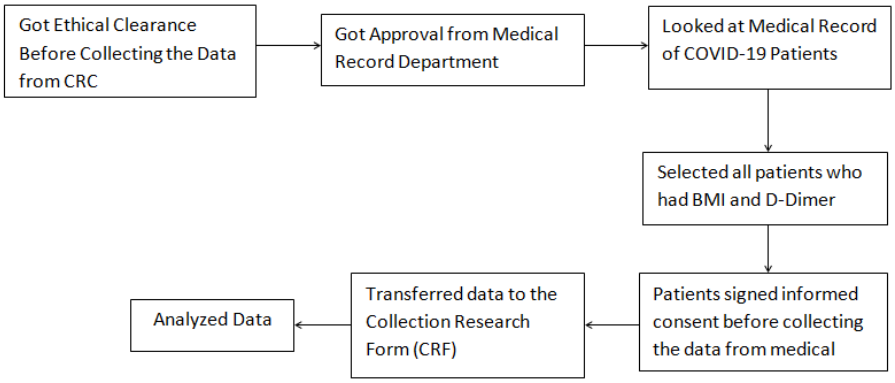

Fig. 1: Research framework of the study

RESULTS AND DISCUSSION

Correlation between socio-demography and D-Dimer of COVID-19 patients

Based on table 1 showed that most 110 female COVID-19 patients had lower D-Dimer; as many as 104 people (52%) and 6 people (3%) had higher D-Dimer. The 90 male COVID-19 patients had D-Dimer, 86 people (43%) lower D-Dimer, and 4 people (2%) higher D-Dimer. Gender does not correlate with the D-Dimer of COVID-19 patients with a P-value of 0.106>0.05.

Furthermore, it is known that out of 190 COVID-19 patients aged 18-84 y (95%) got lower D-Dimer and the 10 patients aged 18-84 y (5%) got higher D-Dimer. Age does not correlate with the D-Dimer of COVID-19 patients with a P-value of 0.222>0.05.

There are more female patients than males infected with COVID-19 [7]. More women than men were also infected with MERS-CoV and SARS-CoV [8]. The decrease in women's susceptibility to viral infections can be caused by the defense of the X chromosome and sexual hormones, which play an essential role in innate and adaptive immunity [9]. Aging is associated with increased morbidity due to a number of autoimmune, degenerative, and vascular diseases [10]. Increased D-dimer levels have been documented in patients experiencing unstable angina and the fragment may stimulate increased fibrinogen production [11].

Correlation between clinical presentation and D-Dimer of COVID-19 patients

Based on table 2, it is known that 190 patients had a normal complication (38%) and had a pneumonia complication (57%) who received a lower D-Dimer. The 10 patients had a normal complication (0.5%) and had a pneumonia complication (4.5%) who received a higher D-Dimer. Complication does not correlate with the D-Dimer of COVID-19 patients with a P-value of 0.092>0.05. That 190 patients had a Bronchopneumonia duplex (12.5%), Pneumonia bilateral (31.5%), Pneumonia dextran (9%), Pneumonia duplex (0.5%), Pneumonia Sinistra (3%), and within normal limits (38.5%) who receive a lower D-Dimer. The 10 patients had a Bronchopneumonia duplex (2%), Pneumonia bilateral (1.5%), Pneumonia dextran (1%), Pneumonia duplex (0%), Pneumonia Sinistra (0.5%), and within normal limits (0.5%) who receive a higher D-Dimer. CT-Scan does not correlate with the D-Dimer of COVID-19 patients with a P-value of 0.134>0.05. The 190 patients who receive lower D-Dimer and 10 patients who receive higher D-Dimer are hospitalized in Non-ICU care. ICU/Non-ICU does not correlate with the D-Dimer of COVID-19 patients. That 183 patients who receive lower D-Dimer (91.5%) get clinical outcomes live, and 7 patients (3.5%) died. The nine patients who received lower D-Dimer (4.5%) got clinical outcomes live, and one patient (0.5%) died. Clinical outcomes do not correlate with the D-Dimer of COVID-19 patients with a P-value of 0.342>0.05. 190 patients had Diabetes mellitus (2.5%), Hypertension (3%), Tuberculosis (0.5%), and without comorbid (89%) who received lower D-Dimer. The ten patients had Diabetes mellitus (0.5%) and without comorbid (4.5%) who received higher D-Dimer. Comorbid does not correlate with D-Dimer of COVID-19 patients with a P-value of 0.552>0.05. The most 190 patients got an antimicrobial as many as 154 people (77%) bacterial and 36 (18%) viral who received lower D-Dimer. The 10 patients got antimicrobial, 9 people (4.5%) bacterial and 1 people (0.5%) viral. Antimicrobial type does not correlate with the D-Dimer of COVID-19 patients with a P-value of 0.692>0.05. That 190 patients had a lower D-Dimer got the grade, as many as 12 people (6%) mild, 8 people (4%) moderate, 1 (0.5%), and 169 people (84.5%) asymptomatic. The 10 patients with a higher D-Dimer got an asymptomatic grade (5%). Grade does not correlate with D-Dimer of COVID-19 patients with a P-value of 0.745>0.05. The most 190 patients who got a medication COVID-19 type had a lower D-Dimer, and 10 patients had a higher D-Dimer. Medication COVID type does not correlate with D-Dimer of COVID-19 patients with a P-value of 0.597>0.05. The most 190 patients who got a comorbid medication type had a lower D-Dimer, and 10 patients had a higher D-Dimer. Medication COVID type does not correlate with D-Dimer of COVID-19 patients with a P-value of 0.997>0.05. The most 190 patients who got a medication injection type had a lower D-Dimer, and 10 patients had a higher D-Dimer. Medication COVID type does not correlate with D-Dimer of COVID-19 patients with a P-value 0.229>0.05.

These results are in keeping with the view that high d-dimer values are seen in association with malignancy and that this parameter may be a valuable trigger to identify patients requiring investigation for underlying COVID-19 [12]. Further studies are necessary to evaluate the clinical usefulness of high d-dimer levels, both at presentation and intervals after that. The concept that the only beneficial d-dimer result within the normal range may not necessarily remain in the future [13]. Furthermore, in this study, serial D-dimer measurements did not help identify patients with clinical improvements or impairments because D-dimer levels in most cases increased throughout the 14th day and even then showed only a modest albeit significant decrease [14].

In a study from Querol-Ribelles *et al.*, 200 patients treated in non-ICU with Pneumonia had high levels of d-dimers. Several researchers have discussed the relationship between d-dimer levels and clinical outcomes in Covid-19 patients [14]. It has also observed similar results in critically ill patients due to severe Pneumonia. In addition, they have found that d-dimer levels are higher in patients with bilateral Pneumonia than in patients with duplex bronchopneumonia [15].

That 190 patients had lower D-Dimer got some values of blood pressure, as many as 103 people (51.5%) average, 54 people (27%) prehypertension, 25 people (12.5%) stage-1 hypertension, 8 people (4%) stage-2 hypertension. The 10 patients had a higher D-Dimer got some values of blood pressure, 5 people (2.5%) average, 4 people (2%) prehypertension, 1 people (0.5%) stage-1 hypertension, and no one got stage-2 hypertension. Blood pressure does not correlate with the D-Dimer of COVID-19 patients with a P-value 0.882>0.05. According to WHO, blood pressure numbers of less than 120/80 mmHg are considered normal. Prehypertension or elevated blood pressure is when readings consistently range from

120-129 systolic and less than 80 mmHg diastolic. Hypertension stage 1 is when blood pressure goes from 130-139 systolic to 80-89 mmHg diastolic. Hypertension stage 2 is when blood pressure consistently ranges at 140/90 mmHg or higher [16].

The most 190 patients had a heart range and pulse got lower D-Dimer (95%), and 10 patients had a heart range and pulse got higher D-Dimer (5%). Heart range and vibration do not correlate with D-Dimer of COVID-19 patients with a P-value of 0.116>0.05. Based on Paul *et al.*, heart rate is separate from blood pressure, that's the force of blood against the walls of blood vessels. Normal resting heart rate is usually between 60 to 100 beats per minute [17]. A faster pulse does not necessarily mean higher blood pressure.

The 190 patients who receive lower D-Dimer got some results from medical records, which is Temperature, Hb, MCV, MCH, MCHC, Lymphocytes, Leukocyte, Erythrocyte, SGOT, SGPT and Glucose (95%) and 10 patients who receive higher D-Dimer (5%). Temperature, Hb, MCV, MCH, MCHC, Lymphocytes, Leukocyte, Erythrocyte and Glucose with D-Dimer of COVID-19 patients with a P-value, which is temperature 0.673>0.05, Hb 0.515>0.05, MCV 0.662>0.05, MCH 0.680>0.05, MCHC 0.718>0.05, Lymphocytes 0.071>0.05, Leukocyte 0.743>0.05, Erythrocyte 0.457>0.05.

According to Palmes *et al.*, average body temperature is considered 37 °C (98.6 °F); however, a wide variation is seen. Normal individuals' mean daily temperature can differ by 0.5 °C (0.9 °F), and daily variations can be as much as 0.25 to 0.5 °C [18]. The nadir in body temperature usually occurs at about 4 am and at about 6 pm. This circadian rhythm is reasonably constant for an individual and is not disturbed by periods of fever or hypothermia [19]. Prolonged change to daytime-sleep and nighttime-awake cycles will affect the circadian rhythm's adaptive correction. Average rectal temperature is typically 0.27° to 0.38 °C (0.5° to 0.7 °F) more significant than an oral temperature. Axillary temperature is about 0.55 °C (1.0 °F) less than the oral temperature [19].

Table 1: Correlation between socio-demography and clinical parameters with D-dimer of COVID-19 patients

Variable	Total n = 200	D-Dimer<500 ng/ml n = 190	D-Dimer>500 ng/ml n = 10	P Value
Gender				0.106
Male	90	86 (43%)	4 (2%)	
Female	110	104 (52%)	6 (3%)	
Age	200	190 (95%)	10 (5%)	0.222
Complication	Normal: 77	Normal: 76 (38%)	Normal: 1 (0.5%)	0.092***
	Pneumonia: 123	Pneumonia: 114 (57%)	Pneumonia: 9 (4.5%)	
Comorbid	DM: 6	DM: 5 (2.5%)	DM: 1 (0.5%)	0.552***
	HTN: 6	HTN: 6 (3%)	HTN: 0	
	TB: 1	TB: 1 (0.5%)	TB: 0	
	Without Comorbid: 187	Without Comorbid: 178 (89%)	Without Comorbid: 9 (4.5%)	
BMI	200	190 (95%)	10 (5%)	0.047*
BB	200	190 (95%)	10 (5%)	0.283*
TB	200	190 (95%)	10 (5%)	0.475*
CT-Scan	Bronchopneumonia duplex: 29	Bronchopneumonia duplex: 25 (12.5%)	Bronchopneumonia duplex: 4 (2%)	0.134**
	P. bilateral: 66	P. bilateral: 63 (31.5%)	P. bilateral: 3 (1.5%)	
	P. dextra: 20	P. dextra: 18 (9%)	P. dextra: 2 (1%)	
	P. duplex: 1	P. duplex: 1 (0.5%)	P. duplex: 0	
	P. sinistra: 6	P. sinistra: 6 (3%)	P. sinistra: 0	
	DBN: 78	DBN: 77 (38.5%)	DBN: 1 (0.5%)	
Antimicrobial Type	Bacterial: 163	Bacterial: 154 (77%)	Bacterial: 9 (4.5%)	0.692***
	Viral: 37	Viral: 36 (18%)	Viral: 1 (0.5%)	
Duration of Treatment	200	190 (95%)	10 (5%)	0.591*
ICU/Non ICU	200	190 (95%)	10 (5%)	-*
Grade	Mild: 12	Mild: 12 (6%)	Mild: 0	0.745***
	Moderate: 8	Moderate: 8 (4%)	Moderate: 0	
	Severe: 1	Severe: 1 (0.5%)	Severe: 0	
	Asimtomatis: 169	Asimtomatis: 169 (84.5%)	Asimtomatis: 10 (5%)	
Medication COVID Type	200	190 (95%)	10 (5%)	0.597*
Medication Comorbid Type	200	190 (95%)	10 (5%)	0.997*
Medication Injection Type	200	190 (95%)	10 (5%)	0.229*
BP	Normal: 108	Normal: 103 (51.5%)	Normal: 5 (2.5%)	0.882***
	Prehypertension: 58	Prehypertension: 54 (27%)	Prehypertension: 4 (2%)	
	Stage-1 Hypertension: 26	Stage-1 Hypertension: 25 (12.5%)	Stage-1 Hypertension: 1 (0.5%)	
	Stage-2 Hypertension	Stage-2 Hypertension: 8 (4%)	Stage-2 Hypertension: 0	
HR	200	190 (95%)	10 (5%)	0.116*
P	200	190 (95%)	10 (5%)	0.116*
T	200	190 (95%)	10 (5%)	0.673*
Hb	200	190 (95%)	10 (5%)	0.515*
MCV	200	190 (95%)	10 (5%)	0.662*
MCH	200	190 (95%)	10 (5%)	0.680*
MCHC	200	190 (95%)	10 (5%)	0.718*
Limfosit	200	190 (95%)	10 (5%)	0.071*
Leukosit	200	190 (95%)	10 (5%)	0.743*
Eritrosit	200	190 (95%)	10 (5%)	0.457*
SGOT	200	190 (95%)	10 (5%)	0.000*
SGPT	200	190 (95%)	10 (5%)	0.000*
SCr	200	190 (95%)	10 (5%)	0.013*
CrCl	200	190 (95%)	10 (5%)	0.012*
Ureum	200	190 (95%)	10 (5%)	0.011*
Glucose	200	190 (95%)	10 (5%)	0.146*
Clinical Outcome	Live: 192	Live: 183 (91.5%)	Live: 9 (4.5%)	0.342***
	Died: 8	Died: 7 (3.5%)	Died: 1 (0.5%)	

In this study by P. Ravi Sarma *et al.*, MCV defines the size of the red blood cells and is expressed as femtoliters (10^{-}[15]; fl) or as cubic microns (μm^3). The normal values for MCV are 87±7 fl. MCH quantifies the amount of hemoglobin per red blood cell. The normal values for MCH are 29±2 picograms (pg) per cell. MCHC indicates the amount of hemoglobin per unit volume. In contrast to MCH, MCHC correlates the hemoglobin content with the cell volume. It is expressed as g/dl of red blood cells or as a percentage value. The normal values for MCHC are 34±2 g/dl [20].

Based on Cong Ma *et al.*, the normal value for erythrocytes for men is 5.0 (4.5-6.0) million and 4.5 (4.3-5.5) million for women. The value for lymphocytes is 1,000-4,000 with a percentage of 20-40%. And for the expected value of leukocytes is 5,000-10,000 with a portion of 100% [21].

Correlation between BMI and D-Dimer of COVID-19 Patients

Based on table 1, it is known that ten patients had high D-Dimer and most patients had low D-Dimer (90%). BMI correlated with D-Dimer for Covid-19 patients with a P value of 0.047<0.05. According to the WHO, body fatness is classified based on body mass index and considered healthy if BMI>18.5, overweight if BMI>25, obesity if BMI>30, and morbid obesity if BMI>40. Weight gain leads to worse metabolic changes in certain ethnic groups. As a result, Asians should be considered overweight if BMI>23 and obese if BMI>27.5 [22].

Correlation between SGOT and SGPT with D-Dimer of COVID-19 patients

Based on table 1, it is known that ten patients had high D-Dimer and most patients had low D-Dimer (90%). SGOT and SGPT correlated with D-Dimer for Covid-19 patients with a P-value of 0.00<0.05. In this study, Jerold A *et al.*, the normal range of AST (SGOT) values is about 5 to 40 units per liter of serum (the liquid part of the blood). And the normal range of values for ALT (SGPT) is about 7 to 56 units per liter of serum [23].

Correlation between serum creatinine, creatinine clearance, and ureum with d-dimer of COVID-19 patients

Based on table 1, it is known that ten patients had high D-Dimer and most patients had low D-Dimer (90%). Serum creatinine correlated with D-Dimer for Covid-19 patients with a P-value of 0.013<0.05. Based on Sottas *et al.*, serum creatinine remained constant for healthy subjects on average between 20 and 70 y of age, with an average of 0.90 mg/dl and normal reference intervals (0.63-1.16 mg/dl) for women (white) and with an average of 0.70 mg/dl and normal reference intervals (0.48-0.93 mg/dl) for women (white) [24]. Over the age of 70, serum creatinine begins to increase again in both sexes slowly. It is said that when a person's serum creatinine levels rise but remain within population-based reference intervals, it may still be an indication as an early warning signal for future kidney dysfunction [24, 25].

Based on table 2, it is known that ten patients had high D-Dimer and most patients had low D-Dimer (90%). Creatinine clearance correlated with D-Dimer for Covid-19 patients with a P-value of 0.012<0.05. According to Brian *et al.*, the creatinine clearance value is determined by measuring the concentration of endogenous creatinine (that which is produced by the body) in both plasma and urine. Reference values for healthy creatinine clearance levels vary by age and sex. In general, reference values for men are in the range of 97–137 ml per minute and for women 88–128 ml per minute. A normal range for newborns usually is between 40 and 65 ml per minute [26].

Based on the table, ten patients had high D-Dimer, and most patients had low D-Dimer (90%). Ureum correlated with D-Dimer for Covid-19 patients with a P-value of 0.011<0.05. From the study of Adrian *et al.*, the normal range of urea nitrogen in the blood or serum is 5 to 20 mg/dl, or 1.8 to 7.1 urea mmol per liter [27]. This range is wide due to normal variations due to protein intake, endogenous protein catabolism, state of hydration, liver urea synthesis, and renal urea excretion. BUN 15 mg/dl will represent a significantly impaired function in women in the thirtieth week of pregnancy [27].

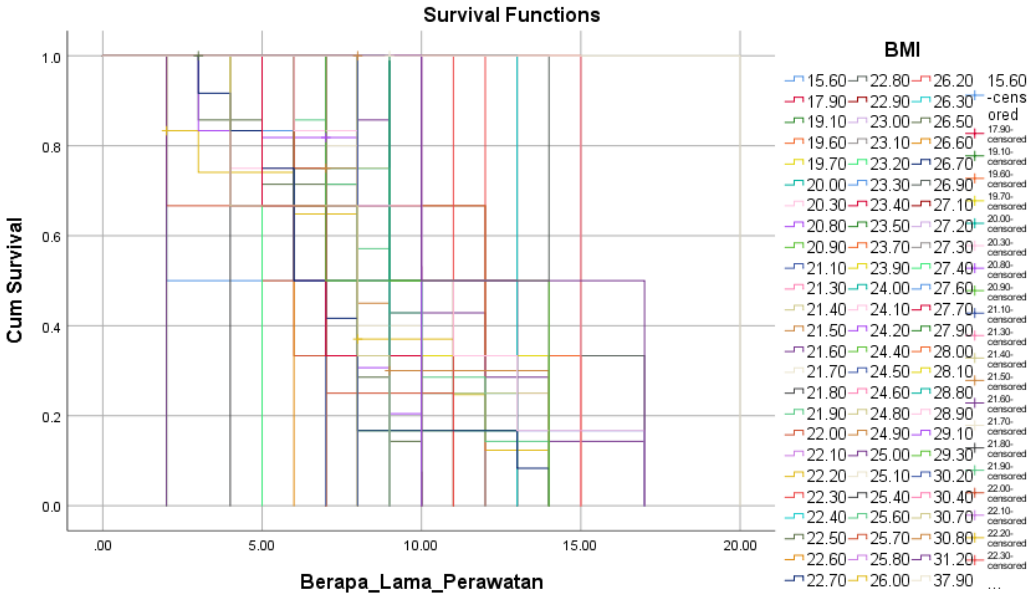

Fig. 2: Survival analysis among COVID-19 patients

Survival analysis among COVID-19 patients

Based on fig. 2, it can be seen that patients who receive underweight BMI had an average survival rate of around 2% after undergoing treatment for around nine days. Patients who receive normal BMI had an average survival rate of around 64% after about 17 d of treatment. Patient receive overweight BMI had an average survival rate of around 30% after around 14 d of treatment. Patient receive obese BMI had an average survival rate of around 4% after approximately 20 d of treatment.

A significant correlation was found among the overall comparisons between survival analysis and BMI of COVID-19 patients. In a research study by Thai *et al.*, The median duration of hospitalization among patients was under 21 d. The multivariable Cox regression model shows that age, residence, and contamination sources are

significantly associated with hospital extended stays [28, 29]. Adjusted multivariate analysis showed that longer length of stay in hospital was associated with a factor of age 45 and more, those who were admitted to a provincial hospital, and those who were seriously ill [30]

CONCLUSION

Almost all COVID-19 patients are still alive, and only 4% of patients died in studies with D-Dimer above 500 ng/ml based on treatment duration. It is known that many of these COVID-19 patients have complications of bacterial Pneumonia by 81.5%. A significant correlation was found between BMI and D-Dimer in COVID-19 patients with a p-value of 0.047<0.05.

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Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Cao X. COVID-19: Immunopathology and its implications for therapy. Nat Rev Immunol. 2020;20(5):269-70. doi: 10.1038/s41577-020-0308-3, PMID 32273594.
2. Fraser N, Brierley L, Dey G, Polka JK, Pálfy M, Nanni F. Preprinting the COVID-19 pandemic; 2021.
3. Weitz JI, Fredenburgh JC, Eikelboom JW. A test in context: D-dimer. J Am Coll Cardiol. 2017;70(19):2411-20. doi: 10.1016/j.jacc.2017.09.024, PMID 29096812.
4. Johnson ED, Schell JC, Rodgers GM. The D-dimer assay. Am J Hematol. 2019;94(7):833-9. doi: 10.1002/ajh.25482, PMID 30945756.
5. Rothman KJ. BMI-related errors in the measurement of obesity. Int J Obes (Lond). 2008;32Suppl 3:S56-9. doi: 10.1038/ijo.2008.87, PMID 18695655.
6. Nuttall FQ. Body mass index: obesity, BMI, and health: A critical review. Nutr Today. 2015;50(3):117-28. doi: 10.1097/NT.0000000000000092, PMID 27340299.
7. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13. doi: 10.1016/S0140-6736(20)30211-7, PMID 32007143.
8. Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, Perlman S. Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection. J Immunol. 2017;198(10):4046-53. doi: 10.4049/jimmunol.1601896, PMID 28373583.
9. Jaillon S, Berthenet K, Garlanda C. Sexual dimorphism in innate immunity. Clin Rev Allergy Immunol. 2019;56(3):308-21. doi: 10.1007/s12016-017-8648-x, PMID 28963611.
10. Pieper CF, Rao KM, Currie MS, Harris TB, Cohen HJ. Age, functional status, and racial differences in plasma D-dimer levels in community-dwelling elderly persons. J Gerontol A Biol Sci Med Sci. 2000;55(11):M649-57. doi: 10.1093/gerona/55.11.m649, PMID 11078094.
11. Currie MS, Rao MK, Blazer DG, Cohen HJ. Age and functional correlations of markers of coagulation and inflammation in the elderly: functional implications of elevated crosslinked fibrin degradation products (D-dimers). J Am Geriatr Soc. 1994;42(7):738-42. doi: 10.1111/j.1532-5415.1994.tb06534.x, PMID 8014349.
12. Deng G, Yin M, Chen X, Zeng F. Clinical determinants for fatality of 44,672 patients with COVID-19. Crit Care. 2020;24(1):179. doi: 10.1186/s13054-020-02902-w, PMID 32345311.
13. Lippi G, Mattiuzzi C, Sanchis Gomar F, Henry BM. Clinical and demographic characteristics of patients dying from COVID-19 in Italy vs China J. J Med Virol. 2020;92(10):1759-60. doi: 10.1002/jmv.25860.
14. Querol Ribelles JM, Tenias JM, Grau E, Querol Borras JM, Climent JL, Gomez E. Plasma d-dimer levels correlate with outcomes in patients with community-acquired Pneumonia. Chest. 2004;126(4):1087-92. doi: 10.1378/chest.126.4.1087, PMID 15486368.
15. Ramatillah DL, Gan SH, Sulaiman SAS, Puja D, Abubakar U, Jaber AAS, Lukas S, Jusnita N. Evaluation of treatment outcome for pneumonia among pre-vaccinated COVID-19 patients with/without comorbidity in a Public Hospital in Bengkulu, Indonesia. Vaccines. 2021;9(12):1411. doi: 10.3390/vaccines9121411, PMID 34960157.
16. Chia YC. Prehypertension: what is the current status? Malays Fam Physician. 2008;3(2):72-6. PMID 25606120.
17. Muntner P, Shimbo D, Carey RM, Charleston JB, Gaillard T, Misra S, Myers MG, Ogedegbe G, Schwartz JE, Townsend RR, Urbina EM, Viera AJ, White WB, Wright JT. Measurement of blood pressure in humans: A scientific statement from the American Heart Association. Hypertension. 2019;73(5):e35-66. doi: 10.1161/HYP.0000000000000087, PMID 30827125.
18. Palmes ED, Park CR. The regulation of body temperature during fever. Arch Environ Health. 1965;11(6):749-59. doi: 10.1080/00039896.1965.10664295, PMID 5846067.
19. Hammel HT. Regulation of internal body temperature. Annu Rev Physiol. 1968;30:641-710. doi: 10.1146/annurev.ph.30.030168.003233, PMID 4871163.
20. GREEN PT. Red cell indices. Manit Med Rev. 1950;30(6):371-2. PMID 15438127.
21. Ma C, Wang X, Zhao R. Associations of lymphocyte percentage and red blood cell distribution width with risk of lung cancer. J Int Med Res. 2019;47(7):3099-108. doi: 10.1177/0300060519850417, PMID 31167586.
22. Setty P, Padmanabha B, Doddamani B. Correlation between obesity and cardiorespiratory fitness. Int J Med Sci Public Health. 2013;2(2):300. doi: 10.5455/ijmsph.2013.2.298-302.
23. Cohen JA, Kaplan MM. The SGOT/SGPT ratio-an indicator of alcoholic liver disease. Dig Dis Sci. 1979;24(11):835-8. doi: 10.1007/BF01324898, PMID 520102.
24. Sottas PE, Kapke GF, Leroux JM. Adaptive Bayesian analysis of serum creatinine as a marker for drug-induced renal impairment in an early-phase clinical trial. Clin Chem. 2012;58(11):1592-6. doi: 10.1373/clinchem.2012.193698, PMID 22991423.
25. Delanaye P, Cavalier E, Pottel H. Serum creatinine: not so simple! Nephron. 2017;136(4):302-8. doi: 10.1159/000469669, PMID 28441651.
26. Nankivell BJ. Abnormal laboratory results: creatinine clearance and the assessment of renal function. Aust Prescr. 2001;24(1):15-7. doi: 10.18773/austprescr.2001.009.
27. Hosten AO. Clinical methods: the history, physical, and laboratory examinations. Ann Intern Med. 1990;113(7):563. doi: 10.7326/0003-4819-113-7-563_2.
28. Ramatillah DL, Isnaini S. Treatment profiles and clinical outcomes of COVID-19 patients at private hospital in Jakarta. PLOS ONE. 2021;16(4):e0250147. doi: 10.1371/journal.pone.0250147. PMID 33861777.
29. Dars S, Sayed K, Yousufzai Z. Relationship of menstrual irregularities to BMI and nutritional status in adolescent girls. Pak J Med Sci. 2014;30(1):141-4. doi: 10.12669/pjms.301.3949, PMID 24639848.
30. Wang Z, Ji JS, Liu Y, Liu R, Zha Y, Chang X. Survival analysis of hospital length of stay of novel coronavirus (COVID-19) pneumonia patients in Sichuan, China. medRxiv. 2020.