Journal of Clinical Virology Plus 2 (2022) 100068

Contents lists available at ScienceDirect

Journal of Clinical Virology Plus

journal homepage: www.elsevier.com/locate/jcvp

Factors associated with death and ICU referral among COVID-19 patients hospitalized in the secondary referral academic hospital in East Jakarta, Indonesia

Kurniyanto[a,*], Yessi Setianegari[a], Linggom Kurniaty[b], Danny E.J. Luhulima[c], Bambang S.R. Utomo[d], Louisa A. Langi[e], Ronny[f], Evy S. Arodes[g], Marwito Wiyanto[h], Eva Suarthana[i], Retno Wahyuningsih[f]

[a] Department of Internal Medicine, Faculty of Medicine, Universitas Kristen Indonesia, Jakarta, Indonesia
[b] Department of Pharmacology and Therapeutic, Faculty of Medicine, Universitas Kristen Indonesia, Jakarta, Indonesia
[c] Department of Clinical Pathology, Faculty of Medicine, Universitas Kristen Indonesia, Jakarta, Indonesia
[d] Department of Otorhinolaryngology, Faculty of Medicine, Universitas Kristen Indonesia, Jakarta, Indonesia
[e] Department of Community of Public Health, Faculty of Medicine, Universitas Kristen Indonesia, Jakarta, Indonesia
[f] Department of Parasitology, Faculty of Medicine, Universitas Kristen Indonesia, Jakarta, Indonesia
[g] Department of Microbiology, Faculty of Medicine, Universitas Kristen Indonesia, Jakarta, Indonesia
[h] Department of Biomedicine, Faculty of Medicine, Universitas Kristen Indonesia, Jakarta, Indonesia
[i] Research Institute of McGill University Health Center, Montreal, Canada

A B S T R A C T

Introduction: : We present demographic and clinical characteristics including laboratory and imaging data of COVID-19. Factors associated with death and ICU referral were evaluated.

Methods: : This is a retrospective cohort study of hospitalized COVID-19 patients confirmed by real time polymerase chain reaction (RT-PCR). Logistic regression was used to evaluate the associations between demographic and clinical characteristics with the outcomes.

Results: : A total of 477 patients have been hospitalized from October 2020 - February 2021, 112 patients were over 60 years old and 58.2% were women. There were 299 (62.7%) patients with clinical improvement and negative RT-PCR at discharge, 145 (30.4%) patients with clinical improvement and positive RT-PCR at discharge, 14 (2.9%) patients referred to ICU, and 19 (4%) patients died. The most common clinical symptoms were fever, cough, nausea and vomiting, and shortness of breath. Multivariate logistic regression analysis revealed age ≥60 years old, shortness of breath, obesity, oxygen saturation <95%, leukocyte count >10,000/L, and moderate-severe COVID-19 at admission were strongly associated with death or referral to ICU.

Conclusion: : Patients aged over 60 years old with obesity, low peripheral oxygen saturation, high leucocyte count, shortness of breath and moderate-severe COVID-19 at admission had higher risks of death or referred to ICU.

1. Introduction

Since the first case of SARS-CoV-2 infection in humans was reported in Wuhan, China in December 2019, Coronavirus disease-19 (COVID-19) has caused the deaths of around 5 million people worldwide [16]. The number of COVID-19 cases in Indonesia alone reached 3.7 million with a death toll of 114,000 as of August 2021 (COVID19.go.id, 2021) [11]. The clinical spectrum of COVID-19 varies from asymptomatic, mild upper respiratory tract infections to severe pneumonia with respiratory failure. Symptoms that patients commonly complain of include fever, cough, and shortness of breath. As many as 5% of cases have hyperinflammatory conditions that cause severe lung damage and ultimately respiratory failure [2]. Mortality in COVID-19 cases is influenced by several factors such as age, obesity, co-morbidities such as diabetes mellitus, hypertension, heart disease, chronic lung disease and liver disease range from 0.5% to 19.3% [12]. Resources to manage critical illnes are also important as seen mortality due to COVID-19, in the low and middle-income countries is high [4]. The general hospital of the Faculty of Medicine of Universitas Kristen Indonesia (UKI) is a secondary referral hospital treating mild-to-moderate COVID-19 patients. Patients are treated according to the management guidelines set by the government [7]. The implementation of these guidelines may differ according to the type of hospital (RS) according to the availability of human resources and health facilities and supporting systems [7].

Research at the secondary referral hospital is still limited, so we conducted a study with the aim of getting an overview of COVID-19 patients treated at this setting The aim of this study is to describe the demographics data, comorbidities, presenting clinical, laboratory tests, imaging, and outcomes of the patient with COVID-19 admitted to a secondary

* Corresponding author.
E-mail address: kurniyanto@outlook.com.

https://doi.org/10.1016/j.jcvp.2022.100068
Received 20 January 2022; Received in revised form 16 February 2022; Accepted 17 February 2022
2667-0380/© 2022 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

referral hospital in Jakarta. Factors associated with death and ICU referral were evaluated.

2. Methods

This study was conducted at UKI Hospital, main academic hospital for Universitas Kristen Indonesia, Faculty of Medicine in Jakarta. This hospital is serving persons living in East Jakarta, but during this pandemic many patients came from other part of Jakarta, such as from South Jakarta, West Jakarta, even from outside Jakarta such as Bekasi, Depok and Bogor.

3. Study design and participants

The study was conducted during the first wave of COVID-19 pandemic in Jakarta during October 2020 to February 2021. This study is a retrospective cohort study that analyzed demographic data, clinical data, and other data (factors) related to morbidity and mortality of COVID-19. The population of this study was all patients confirmed to have COVID-19 who were admitted to the UKI General Hospital during that period. The clinical specimens for the diagnosis of COVID-19 were taken from nasopharyngeal and or oropharyngeal swabs which were tested by KIT BG SARS-COV-2RT-PCR (General Biological Corporation, cat. number 4PCO052E, Taiwan) according to the manufacturer's instructions.

4. Data collection

The data of this study were obtained from medical records of patients which include the demographic information's, symptoms, comorbidities, length of stay in the COVID-19 isolation room, laboratory results e.g., complete blood count, blood sugar, aspartate transaminase (AST), Alanine transaminase (ALT), urea, creatinine, C-reactive protein (CRP), D-dimer, results of microbiological examination of oropharyngeal swabs, radiological imaging results, treatment, and clinical outcomes. Comorbid data is obtained from medical records based on examination when the patient was admitted to the hospital and or based on the patient's medical history statement. Based on clinical outcomes, patients were grouped into four groups: group-1 was patients with clinical improvement and negative real time polymerase chain reaction (RT-PCR) when discharged; group-2 patients with clinical improvement with positive RT-PCR results when discharged; group-3 is patients who require intensive care unit (ICU) and was referred to other hospitals with ICU facilities for COVID-19, and group-4 is deceased patients.

5. Statistical analysis

Descriptive analysis was conducted to determine the distribution of patient characteristics. Categorical variables are displayed in percentage form. Numeric variables will be displayed in the mean (standard deviation) or median (interquartile range or IQR). Univariate analysis was performed to assess the relationship between the four categories of clinical outcomes with demographic characteristics, clinical data, laboratory data, other supporting examinations, and therapy given. Because the data distribution was not normal, Kruskal Wallis' test was used to compare the median of numerical variables, while Chi-Square test or Fisher's exact test was used for categorical variables. Univariate analysis was also performed to compare the characteristics of the clinical improvement group by RT-PCR negative vs. RT-PCR positive. Since the data distribution was not normal, the Mann-Whitney test was used to compare the median of numerical variables, while the Chi-Square test or Fisher's exact test was used for categorical variables. Multivariate analysis using logistic regression was performed to determine the characteristics that were most strongly associated with clinical outcomes. For logistic regression analysis, the outcomes were divided into two categories, namely clinical improvement vs. referral to ICU or death due to the small number of patients in the last category. All characteristics that have a univariate value of $P<0.10$ were included in the multivariate analysis. The value of $p<0.05$ was significant. Statistic analysis were using SPSS version 26.

6. Results

From October 2020 - February 2021, 477 COVID-19 patients were hospitalized at UKI General Hospital, Jakarta. The diagnosis of COVID-19 was confirmed by an RT-PCR examination of a nasopharyngeal swab or oropharyngeal swab. A total of 208 of the 477 study subjects were male and 112/477 were included in the elderly group aged over 60 years. The age range of the studied patients ranged from 5 to 83 years (IQR 37.0, 59.0) and 11 children aged <18 years.

Based on the grouping of patients, Group-1 was 299 (62.7%), Group-2 was 145 patients (30.4%), Group-3 (referred) was 14 patients (2.9%) and Group-4 (died) was 19 patients (4.0%). In Group-1, 18.4% were elderly over 60 years and 58.5% were women. The median and IQR length of stay (LOS) of patients in the COVID-19 isolation room was 12 days (IQR 9.0, 15.0). The most common symptoms were fever (81.9%), followed by cough (74.9%), nausea and vomiting (68.2%), and shortness of breath (38.4%). Almost all patients (99.7%) were conscious on admission to the emergency unit and half (51.5%) had rhonchi on physical examination. The median oxygen saturation of the patient at the first admission to the emergency unit was 97% (95% IQR, 98%). The most common comorbidities were hypertension (42.8%) followed by diabetes (18.1%) and obesity (20.7%). Median C-reactive protein (CRP) test results were 25.0 (IQR 13.2, 117.9) and D-dimer 394.5 (IQR 270.0, 658.3). The results of other laboratory tests such as complete blood count, blood glucose, AST, ALT, urea, creatinine, CRP, and D-dimer in Group-1 patients were still within normal limits (Table 1). Ground-glass opacity (GGO) on the CT scan of the thorax was found in 54.5% of patients while the median CT value was 27.5 (IQR 22.5, 32.7). Most patients in Group-1 belonged to mild-moderate COVID-19, as many as 44.1–51.2% (Table 1). Favipiravir was administered to (66.2%) patients and 19.1% of patients were not taking antivirals. A total of 35.5% of patients received dexamethasone, while 58.2% of patients did not use steroids. In Group-1, 75.9% of patients were not taking anticoagulants (Table 3).

When Group-2 (145 patients) was compared with Group-1, there were several significant differences. Among others, rhonchi on physical examination (63.4%) and ground-glass opacity on the CT scan of the thorax (65.5%) were more common in Group-2. But the platelet and neutrophil count in Group-2 were significantly lower than Group-1. Many patients in Group-2 (67.6%) were classified as moderately symptomatic COVID-19 and received more dexamethasone as steroid therapy of choice (Table 3).

Group-3 (referred to the COVID-19 referral hospital) consisted of 14 patients. A total of 78.6% of patients were elderly (over 60 years) and the most common symptoms were fever (92.3%), cough (71.4%), dyspnea (71.4%), nausea, and vomiting (64.3%). A total of 21.4% of patients came with alter consciousness, rhonchi (85.7%) on physical examination and, the patient's oxygen saturation upon admission to the emergency unit was 93.0% (IQR 86.3%, 97.3%). The CT scan of the chest showed ground-glass opacity (85.7%) and crazy paving (42.9%) and these results were higher compared with Group-1 and Group-2. The most frequent comorbidities were hypertension (64.3%, 9) and obesity (50.0%). The results of laboratory investigations showed the value of C-reactive protein was 198.8 (IQR 34.0, 217.1) and D-dimer 519.0 (IQR 236.5, 1460.0), these results were higher than the patients with good clinical outcomes (Group 1 and 2). Most patients (57.1%) in Group-3 were classified as having severe COVID-19 symptoms (Table 1). In the isolation room, antiviral drug favipiravir was administered to 78.6% of patients. As much as 14.3% of patients were not used steroids and 35.7% of patients were not receiving anticoagulants (Table 3).

Twelve out of 19 patients who died (Group-4), were over 60 years old and 10/19 of them were women. Most patients complained of cough

Table 1
Distribution of sociodemographic and clinical characteristics at admission by the COVID-19 outcome, $n = 477$.

Characteristics	Missing values	Group-1 Recovered, negative swab ($n = 299$) n (%)	Group-2 Recovered, positive swab ($n = 145$) n (%)	Group-3 Referred to ICU ($n = 14$) n (%)	Group-4 Died ($n = 19$) n (%)	*P* value[a]
Demographic Characteristic	0 / 0 / 0 / 0					
Age, year **median (25th; 75th percentiles)**		46.0 (35.0,55.5)	48.0 (37,59.5)	62.5 (61.0, 67.0)	64.0 (56.0,71.5)	<0.001
Age >60 year **n (%)**		55.0 (18.4)	34.0 (23.4)	11.0 (78.6)	12.0 (63.2)	<0.001
Female **n (%)**		175.0 (58.5)	78.0 (53.8)	6.0 (42.9)	10.0 (52.6)	0.55
Length of hospital stay **median (25th; 75th percentiles)**		12.0 (9.0, 15.0)	11.0 (9.0,14.0)	6.0 (1.0, 7.3)	2.0 (1.0, 4.0)	<0.001
Clinical characteristics, n (%)						
Symptoms	0 / 0 / 0 / 0					
Cough	x	224 (74.9)	116 (80)	10 (71.4)	17 (89.5)	0.67
Nasal Congestion	x	61 (20.4)	31 (21.4)	2 (14.3)	2 (10.5)	0.24
Dyspnea	y	104 (34.8)	52 (35.9)	10(71.4)	16 (84.2)	<0.001
Fever	x	245 (81.9)	117 (80.7)	13 (92.9)	15 (78.9)	0.63
Headache	y	111 (37.1)	55 (37.9)	7 (50.0)	8 (42.1)	0.78
Myalgia	y	89 (29.8)	46 (31.7)	4 (28.6)	5 (26.3)	0.95
Nausea, Vomiting	y	204 (68.2)	94 (64.8)	9 (64.3)	9 (47.4)	0.23
Anosmia	x	30 (10.0)	14 (9.7)	3 (21.4)	3 (15.8)	0.14
Ageusia	x	13 (4.3)	2 (1.4)	1 (7.1)	3 (15.8)	0.03
Diarrhea	x	24 (8)	8 (5.5)	2 (14.3)	0 (0.0)	1.00
Sore throat	x	24 (8)	9 (6.2)	2 (14.3)	3 (15.8)	0.17
Skin rash	x	4 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1.00
Chest pain	x	6 (2.0)	4 (2.8)	0 (0.0)	3 (15.8)	0.54
Consciousness	x					
Conscious		298 (99.7)	145 (100)	11 (78.6)	14 (73.7)	<0.001
Unconscious		1 (0.3)	0 (0.0)	3 (21.4)	5 (26.3)	
Rhonchi	y	154 (51.5)	92 (63.4)[c]	12 (85.7)	19 (100)	<0.001
Comorbidities, n (%)	0 / 0 / 0 / 0					
Asthma		8 (2.7)	2 (1.4)	0 (0.0)	0 (0.0)	1.00
Diabetes	x	54 (18.1)	30 (20.7)	2 (14.3)	12 (63.2)	0.001
Hypertension	y	128 (42.8)	67 (46.2)	9 (64.3)	14 (73.7)	0.03
Coronary artery disease	x	9 (3.0)	4 (2.8)	1 (7.1)	2 (10.5)	0.91
Congestive heart failure	x	5 (1.7)	3 (2.1)	0 (0.0)	5 (26.3)	0.001
Chronic kidney disease	x	9 (3.0)	4 (2.8)	1 (7.1)	8 (42.1)	<0.001
Obesity	x	62 (20.7)	37 (25.5)	7 (50.0)	9 (47.4)	<0.001
Vital Sign, median (25th; 75th percentiles)	0 / 0 / 0 / 0					
Systolic blood pressure		134.0 (121.0, 150.0)	135.0 (120.0, 151.5)	138.5 (130.8, 163.5)	143.0 (120.0, 160.0)	0.24
Diastolic blood pressure		82.0 (75.0, 90.0)	83.0 (72.5, 91.0)	84.5 (77.8, 104.0)	70.0 (67.0, 80.0)	0.01
Heart rate, beats/min		90.0 (81.0,100.0)	91.0 (82.0, 100.0)	100.0 (92.8, 113.8)	94.0 (86.0, 113.0)	0.02
Temperature (°C)		37.7 (36.9, 38.4)	37.6 (36.9, 38.3)	37.5 (36.7, 38.5)	37.3 (36.7, 38.2)	0.53
Respiratory rate, breath/min		20.0 (20.0, 22.0)	20.0 (20.0, 22.0)	24.0 (20.0, 27.3)	28.0 (24.0, 30.0)	<0.001
Lowest oxygen saturation measured by pulse oximetry (%)		97.0 (95.0, 98.0)	97.0 (96.0, 98.0)	93.0 (86.3, 97.3)	89.0 (81.0, 94.0)	<0.001
Baseline chest radiograph finding, n (%)	0 / 0 / 0 / 0					
Ground glass opacity	y	163 (54.5)	95 (65.5)[c]	12 (85.7)	18 (94.7)	<0.001
Crazy paving	x	67 (22.4)	32 (22.1)	6 (42.9)	9 (47.4)	0.003
Laboratory finding, median (25th; 75th percentiles)						
Haemoglobin		13.5 (12.6, 14.4)	13.5 (13.0, 14.4)	13.5 (13.0, 14.3)	12.5 (11.0, 14.1)	0.12
Platelet		252,000.0 (199,000.0, 318,000.0)	217,000.0 (188,500.0, 276,500.0) [c]	222,500.0 (128,000.0, 255,500.0)	233,000.0 (181,000.0, 2,888,000.0)	0.004
White blood cell count, cell/uL		7300.0 (5500.0, 8900.0)	6500.0 (5200.0, 9050.0)	9700.0 (6675.0, 13,800.0)	11,500.0 (7300.0, 27,500.0)	<0.001
Neutrophil		67.0 (59.0, 75.0)	63.0 (56.0, 71.5) [c]	80.0 (69.8, 89.3)	83.0 (74.0, 90.0)	<0.001
Lymphocyte		24.0 (18.0, 32.0)	27.0 (20.0, 34.0)	15.0 (5.8, 21.3)	12.0 (3.0, 19.0)	<0.001
Monocyte		5.0 (3.0, 7.0)	5.0 (3.0, 7.0)	4.0 (2.0, 5.8)	4.0 (3.0, 8.0)	0.57
Erythrocyte sedimentation rate	0 / 0 / 0 / 0	40.0 (21.0, 67.0)	38.0 (24.0, 58.0)	62.0 (35.0, 105.5)	68.0 (55.0, 105.0)	<0.001
CRP	238/119/15/7	25.0 (13.2, 117.9)	25.9 (6.4, 111.9)	198.8 (34.0 217.1)	150.9 (43.4, 277.2)	0.04
D-dimer	237/119/17/8	394.5 (270.0, 658.3)	379.5 (214.0, 637.8)	519.0 (236.5, 1460.0)	2022.0 (532.0,-)	0.37
Ureum	0/1/0/0	29.0 (22.0, 38.0)	30.0 (23.3, 40.0)	50.0 (27.8, 136.8)	104.0 (57.0, 144.0)	<0.001
Creatinine, mg/dL	0/0/0/0	0.1 (0.8, 1.2)	1.0 (0.8, 1.2)	1.5 (1.1, 3.9)	1.7 (1.3, 4.7)	<0.001
Aspartate transaminase, IU/L	38/13/3/1	33.5 (21.0, 50.0)	30.0 (21.0, 44.0)	21.0 (20.5, 45.5)	35.5 (26.8, 42.5)	0.004
Alanine transaminase	39/14//3/1	33.5 (21.0, 50.0)	30.0 (21.0, 44.0)	21.0 (20.5, 45.5)	35.5 (26.8, 42.5)	0.46
Blood Glucose		109.0 (93.0, 138.0)	107.0 (94.0, 135.5)	128.0 (115.0, 180.8)	214.0 (129.0, 281.0)	<0.001
CT-value	183/56/6/6	27.5 (22.5, 32.7)	25.9 (19.9. 33.2)	25.0 (22.0, 32.3)	25.2 (21.2, 29.9)	0.63
Severity of COVID-19 disease, n (%)						
Asymtomatic		3 (1.0)	0 (0)	0 (0)	0 (0)	<0.001
Mild		132 (44.1)	46 (37.1)	1 (7)	0 (0)	
Moderate		153 (51.2)	98 (67.6)	5 (35.7)	5 (26.3)	
Severe		11 (3.7)	1 (0.7)	8 (57.1)	14 (73.7)	

b Comparison between recovered vs. dead or referred to ICU.
[a] Comparison between the four groups except stated otherwise
[c] Significantly different from the swab negative group ($P<0.05$)

Table 2
Multivariate logistic regression for death or referred to ICU.

					95% CI	
		B	*P*-value	Exp(B)	Lower	Upper
Full Model	Age >60 years	1.958	<.001	7.083	2.612	19.207
	Dyspnea	1.128	.038	3.090	1.064	8.972
	Obese	1.260	.011	3.527	1.338	9.297
	History of Diabetes Melitus	.479	.319	1.615	.629	4.145
	History of Hypertension	−.100	.848	.905	.327	2.504
	Moderate to severe Illness	2.157	.097	8.647	.674	110.892
	DBP >90 mmHg	−1.006	.100	.366	.110	1.214
	HR >100/min	.681	.176	1.975	.738	5.288
	SpO2 <95%	1.412	.004	4.106	1.562	10.793
	Platelet >450 K /mcL	.802	.436	2.229	.296	16.765
	Leukocyte >10 K /mcL	1.653	<.001	5.222	2.001	13.631
	Ground Glass Opacity on lung CT scan	.188	.824	1.206	.230	6.314
	Crazy Paving on lung CT scan	−.354	.474	.702	.267	1.848
	Constant	−7.603	<.001	.000		
Final Model	Age >60 years	1.670	<.001	5.311	2.178	12.949
	Dyspnea	1.047	.044	2.850	1.027	7.907
	Obese	.999	.028	2.716	1.117	6.601
	Moderate to severe Illness	2.395	.026	10.966	1.329	90.458
	SpO2 <95%	1.377	.003	3.964	1.589	9.886
	Leukocyte >10 K /mcL	1.872	<.001	6.500	2.603	16.230
	Constant	−7.453	<.001	.001		

Table 3
Distribution of treatment by the COVID-19 outcome.

Characteristics	Missing values	Group-1 Recovered, negative swab (*n* = 299)	Group-2 Recovered, positive swab (*n* = 145)	Group-3 Referred to ICU (*n* = 14)	Group-4 Died (*n* = 19)	*P* value[a]
Treatment, n (%)	0 / 0 / 0 / 0					
Antiviral						
Favipirapir		198 (66.2)	106 (73.1)	11 (78.6)	10 (52.6)	0.50[b]
Oseltamivir		23 (7.7)	6 (4.1)	0 (0.0)	0 (0.0)	
Remdesivir		21 (7.0)	16 (11)	1 (7.1)	7 (36.8)	
Not use		57 (19.1)	17 (11.7)	2 (14.3)	2 (10.5)	
Steroid						
Dexamethasone		106 (35.5)	63 (43.4)	7 (50)	12 (63.2)	<0.001
Methylprednisolone		10 (3.3)	8 (5.5)	4 (28.6)	2 (10.5)	
Hydrocortison		9 (3.0)	8 (5.5)	1 (7.1)	4 (21.1)	
Not use		174 (58.2)	66 (45.5) [c]	2 (14.3)	1 (5.3)	
Anticoagulant						
Heparin		25 (8.4)	12 (8.3)	1 (7.1)	6 (31.6)	<0.001[b]
Enoxaparin		46 (15.4)	22 (15.2)	8 (57.1)	12 (63.2)	
Antiplatelet		1 (0.3)	1 (0.7)	0 (0.0)	0 (0.0)	
Not use		277 (75.9)	110 (75.9)	5 (35.7)	1 (5.3)	

[a] Comparison between the four groups except stated otherwise.
[b] Comparison between recovered vs. dead or referred to ICU.
[c] Significantly different from the swab negative group ($P<0.05$).

17/19, shortness of breath 16/19, fever 15/19, nausea, and vomiting 9/19. Comorbidities include hypertension 14/19, diabetes 12/19, obesity 9/19, chronic kidney disease 8/19, congestive heart failure 5/19, and coronary artery disease 2/19. Five patients of this group were admitted to the emergency unit with altered consciousness. Shortness of breath was more pronounced in this group with a median respiratory rate of 28 breaths/minute (IQR 24.0, 30.0) and the median of oxygen saturation was 89% (IQR 81%, 94%). Meanwhile, on chest CT thorax, ground-glass opacity was found in 18/19 patients and crazy paving in 9/19 patients. The results of laboratory tests i.e., CRP, D-dimer, and urea values were higher than the other three groups (Table 1). The median length of patient care in the COVID-19 isolation room was two days (IQR 1.0, 4.0). Fourteen out of 19 patients who died were classified among severe COVID-19 symptoms (Table 1). Most patients in this group received antivirals (89.5%), steroids (94.8%), and anticoagulants (94.8%) (Table 3).

The results of the logistic regression test in all subjects (Table 2) showed that the elderly, complained of shortness of breath, obesity, oxygen saturation levels below 95%, had leukocyte values more than10.000/μL and were generally classified as moderate-severe symptoms were the most strongly associated factors and were more at risk for referral to the ICU or death.

There were several factors important in the course of the disease (Table 1). The most important factors were aging (odds ratio 5.3 and 95% CI 2.2, 12.9), severely ill patients (odds ratio of 10.9 and 95% CI 1.3, 90.4), and leukocyte levels more than 10,000/μL (odds ratio of 6.5; 95% CI 2.6, 16.2) were important factors that determine death or to be referred to ICU.

Pulmonary crackles and ground-glass opacity and steroid therapy had a univariable value of $p<0.001$ but were not included in the multivariate analysis because almost all those who died/refferred had rales and GGO or received steroid therapy.

7. Discussion

This study is a clinical - epidemiological study of COVID-19, the infection caused by SARS COV-2, and also a retrospective cohort study that examines clinical and epidemiological data on COVID-19 patients at the secondary refferal and teaching hospital in East Jakarta. This hospital has isolation room facilities for COVID-19 but does not have an

intensive care unit (ICU) and special ventilator for COVID-19 treatment, so patients who require intensive treatment were referred to hospitals that have these facilities. The study was conducted on 477 hospitalized patients who were proven to have COVID-19 by RT-PCR. Most of the patients treated were included in the group of patients with mild to moderate symptoms (Groups 1 & 2) while the rest were patients with moderate to severe symptoms and had to be referred to a referral hospital or died. The clinical spectrum of SARS-COV2 infection can be asymptomatic to critical illness. Symptoms that patients complained about in this study were fever, cough, sore throat, runny nose, and shortness of breath. The clinical diagnosis of pneumonia (76.1%) indicated a moderate to severe clinical category with the most common clinical features being fever, cough, and shortness of breath, Guan et al [5] and Chen et al [3]., in China found the same results.

The patients studied represent the population in East Jakarta due to the location of the hospital. However, due to the soaring number of COVID-19 cases, there is a shortage of inpatient rooms in various hospitals in Jakarta, so that patients at the hospital also come from areas outside East Jakarta and even come from other provinces. Most of the treated patients were women of various ages with a median (IQR) of 48 years. Clinical deterioration and patient mortality were found mainly in the age group above 60 years, but there were no significant differences related to gender. Several studies have stated that men over 50 have a higher risk of clinical deterioration [1, 9]. Another study conducted in Jakarta by Suhendra et al [14]., showed the different results with our study that deaths from COVID 19 were higher in the elderly and males. While in our study, death case were dominated by female ($p = 0.55$) aged over 60 years old with most of them had diabetes and hypertension.

This study has a smaller number of patients compared to other studies. As of 11 patients under 18 years of age generally had mild symptoms with the most symptoms being fever, runny nose, and cough. Comorbidity in SARS-COV 2 infection can worsen the clinical outcome [1]. The most common comorbidities of this study were hypertension, followed by obesity, diabetes mellitus, etc. (Table 1.). Patients over 60 years with comorbidities had a high risk of death, although in multivariate logistic regression only obesity was significant. The risk of death and the need for intensive care was also found in patients who with respiratory distress on admission as indicated by low peripheral oxygen saturation and predominant rales distribution.

In this study, most of the patients who died or were referred to hospitals that had COVID-19 isolation ICU facilities (Groups 3 and 4) were elderly patients (over 60 years), had comorbid hypertension, diabetes, and obesity and a low oxygen saturation on admission and classified as moderate to severe COVID-19 symptoms. Laboratory tests for CRP and D-dimer also showed high results. Increased risk of in-hospital death related to old age plus one or more comorbidities. Peron et al [10]., mentioned COVID-19 disease may rapidly develop into severe acute respiratory syndrome (SARS) in elderly subjects (>60-year-old), especially in those with comorbidities, such as hypertension, diabetes, and pulmonary diseases.

Obesity is a comorbidity that is strongly associated with increase mortality and poor prognosis. This is due to the high concentration of ACE-2 receptors in obesity [15]. The ACE-2 receptor is known as a co-receptor for the entry of the SARS-COV-2 virus and is expressed in various organs of the body [6, 15]. According to Jia et al [6]. the increase of the ACE-2 receptor expression can be found in adipose tissue. This means that the more adipose tissue, the more ACE-2 receptors that can bind to SARS COV-2. Chronic inflammation in obesity is seen with an increase in interleukin 6 (IL-6), adipokines, and proinflammatory cytokines, induces chronic mild inflammation and reduces the immune response [6, 15].

Most of the patients showed good clinical outcomes. Of the 477 patients, most showed clinical improvement and were discharged in good health (93%). Some went home with negative PCR and some were still positive but clinically no symptoms were found. According to WHO (as of 19 September 2021), the mortality rate for COVID-19 in the world is 2%, in China it is 3.77–5.4% and in Indonesia, it is 3.3% [17, 18]. Deaths due to COVID 19 in this study is 3.9%, while patients who were referred to the intensive care unit at the referral hospital were 3%. The mortality rate for COVID-19 patients at UKI general hospital is almost the same as the national mortality rate, although this hospital does not yet have standardized intensive care facilities, and it causes a small number of patients to be referred to more complete health facilities. The clinical outcome of the referred patient is unknown. Similarly, laboratory tests such as erythrocyte sedimentation rate and C-reactive protein levels were higher than in Groups 1 and 2 (p 0.04), lower platelet levels, higher leukocytes, higher neutrophils, and lower lymphocytes, creatinine levels and higher blood sugar. The study of Li et al [8]., reports an increase of D-dimer in the group of severely ill, but from this study, there was no significant difference in terms of the D-dimer levels in the four study groups. The distribution of ground-glass opacity and crazy paving was also higher in groups 3 and 4. The median time from the start of treatment to the patient's death was also 2 days shorter.

Treatment of COVID-19 range from symptomatic in mild disease, antiviral in moderate and severe disease, immune suppresion in inflammatoric stage and anticoagulant in moderate to severe cases. However, until this study was conducted, none of antivirals were definite againts infection of SARS-COV2.[6] In this study we found out there were no different in term of antivirals utilization, with most of the cases used favipiravir. However there were significant different in corticosteroid which dexamethasone being the most prescribed. Administration of anticoagulant was lower in this study due to majority of cases were mild.

The COVID-19 death rate at UKI Hospital is low, only 19 out of 477 patients. Suhendra et al [14]., reports the mortality rate of COVID-19 from 55 hospitals in Jakarta in 2021 was 12%, while in the United States the mortality rate reached 21%. In both studies, the age of the population had a wider range than in this study [13]. Furthermore, the data of Suhendra et al [14]. was coming from the Jakarta Health Office which is a collection of data from various types of hospitals with different facilities, so they cannot be compared with this study. The lower mortality in this study may be due to data collected from one center with most patients were younger (under 60 years) and admitted to the emergency unit with mild COVID-19 symptoms.

8. Limitation

This study has four limitations. First, the patients only came from a single hospital in Jakarta, and hence, it might not represent Covid-19 patients in Jakarta or Indonesia as a whole. Secondly, this is a retrospective study where clinical details of the patients were based on medical record data. Thirdly, not all patients could be followed up until the they were discharged from the hospital. The clinical outcome of those who were referred was unknown. Finally, because the number of subjects was small, especially groups 3 and 4, the conclusions are drawn were not strong.

9. Conclusion

In conclusion, this study found out most cases were female with hypertension, obesity and diabetes mellitus as the most prominent comorbidities. The most symptoms complained were fever, cough and nausea. In term of laboratory results, higher erythrocyte sedimentation rate and CRP, lower platelet count and higher leucocyte count were seen in severe groups. Distribution of ground glass opacity and crazy paving in thoracic imaging were common in severe groups. This study reveal a mortality rate of 3.9%. The majority of the death cases were older than 60 years old with poor clinical and laboratory characteristic at admission. Patients aged over 60 years old with obesity, low peripheral oxygen saturation below 95%, high leucocyte count (more than 10.000/μL), shortness of breath and moderate-severe COVID-19 at admission had higher risks of death or referred to intensive care unit. This results of our study also confirmed numerous studies previously which

highlighted early severe clinical symptoms, laboratory and imaging abnormality for the risk of mortality in patients with COVID-19.

Consent for publication

Not applicable
Abbreviations

Authors contribution

K is responsible for the patient during their hospitalization and writing the paper. RW design of the study, analyzed the data and writing the paper. ES analyzed the data, doing statistical analysis and writing the paper, All authors read and approved the final manuscript.

Funding

This study was funded by Universitas Kristen Indonesia, grant No.022/UKI.R1.5/PPM.2.4/Kontrak Penelitian/2021. The funders of this study have no role in research design, data collection, data analysis, interpretation of data results, or writing of study reports. The authors have full access to all data and are responsible for publication.

Declaration

Ethics

This study was approved by the ethic committee of the Faculty of Medicine, Universitas Kristen Indonesia Jakarta (No. 14/ Etik Penelitian/FKUKI/2021) and, considered as minimal risk research since the data was collected from routine clinical practice and waive the necessities of informed consent.

Declaration of Competing Interest

The authors declare that they have no competing interest

References

[1] M. Biswas, S. Rahaman, T. Biswas, H.Z K, B Ibrahim, Association of sex, age, and comorbidities with mortality in COVID-19 patients: a systematic review and meta-analysis, Intervirology 64 (2021) 36–47, doi:10.1159/000512592.

[2] Center for System Science and Engineering: John Hopkins Coronavirus resource Center, 2021 Available from https://coronavirus.jhu.edu/map.html Accessed 05 October 2021.

[3] R. Chen, W. Liang, M. Jiang, W. Guan, C. Zhan, T. Wang, et al., Risk factors of fatal outcome in hospitalized subjects with coronavirus disease 2019 from a nationwide analysis in China, Chest 158 (1) (2020) 97–105, doi:10.1016/j.chest.2020.04.010.

[4] E. Dong, H. Du, L. Gardner, An interactive web-based dashboard to track COVID-19 in real time, Lancet Infect. Dis. 20 (5) (2020) 533–534, doi:10.1016/S1473-3099(20)30120-1.

[5] W. Guan, Z. Ni, Hu Yu, W. Liang, C. Ou, J. He, et al., Clinical characteristics of coronavirus disease 2019 in China, N. Engl. J. Med. 382 (2020) 1708–1720, doi:10.1056/NEJMoa2002032.

[6] Jia X., Yin C., Lu S., Chen Y., Liu Q., Bai J., et al. Two things about COVID-19 might need attention. Preprints org 2020; doi: 10.20944/preprints202002.0315.v1.

[7] Kementerian Kesehatan Repubik Indonesia, Pedoman pencegahan dan pengendalian coronavirus disease (COVID-19) revisi ke-5, Jakarta: Kementerian Kesehatan Republik Indonesia (Juli 2020) 91–92.

[8] J. Li, Z. Liu, G. Wu, M. Yi, Y. Chen, K. Li, et al., D-Dimer as a prognostic indicator in critically ill patients hospitalized with COVID-19 in Leishenshan Hospital, Wuhan, China, Front. Pharmacol. 11 (2020) 600592, doi:10.3389/fphar.2020.600592.

[9] H. Peckham, N.M. de Gruijter, C. Raine, A. Radziszewska, C. Ciurtin, L.R. Wedderburn, et al., Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission, Nat. Commun. 11 (1) (2020) 6317, doi:10.1038/s41467-020-19741-6.

[10] J.P.S. Peron, H. Nakaya, Susceptibility of the elderly to SARS-CoV-2 infection: ACE-2 overexpression, shedding, and antibody-dependent enhancement (ADE), Clinics (Sao Paulo) 75 (2020) e1912, doi:10.6061/clinics/2020/e1912.

[11] Peta sebaran COVID-19 di Indonesia. Available from https://covid19.go.id/peta-sebaran. Accessed 05 October 2021.

[12] N. Pouw, J. van de Maat, K. Veerman, J.T. Oever, N. Janssen, E. Abbink, et al., Clinical characteristics and outcomes of 952 hospitalized COVID-19 patients in The Netherlands: a retrospective cohort study, PLoS ONE 16 (3) (2021) e0248713, doi:10.1371/journal.pone.0248713.

[13] S. Richardson, J.S. Hirsch, M. Narasimhan, J.M. Crawford, T. McGinn, K.W. Davidson, et al., Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area [published correction appears in JAMA 2020;26;323(20):2098], JAMA 323 (20) (2020) 2052–2059, doi:10.1001/jama.2020.6775.

[14] H. Suhendra, I.R. Elyazar, B.A. Djaafara, L.L. Ekawati, K. Saraswati, V. Adrian, et al., Clinical characteristics and mortality associated with COVID-19 in Jakarta, Indonesia: a hospital-based retrospective cohort study, Lancet Reg. Health West Pac. 9 (2021) 100108, doi:10.1016/j.lanwpc.2021.100108.

[15] A. Tamara, D.L. Tahapary, Obesity as a predictor for a poor prognosis of COVID-19: a systematic review, Diabetes Metab. Syndr. 14 (4) (2020) 655–659, doi:10.1016/j.dsx.2020.05.020.

[16] WHO Weekly epidemiological Update On COVID-19 - 2 November 2021. Available from https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19-2-november-2021..

[17] J. Zhang, X. Wang, X. Jia, J. Li, K. Hu, G. Chen, et al., Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China, Clin. Microbiol. Infect. 26 (6) (2020) 767–772, doi:10.1016/j.cmi.2020.04.012.

[18] G. Zhang, C. Hu, L. Luo, F. Fang, Y. Chen, J. Li, et al., Clinical features and short-term outcomes of 221 patients with COVID-19 in Wuhan, China, J. Clin. Virol. 127 (2020) 104364, doi:10.1016/j.jcv.2020.104364.