Predictor of Mortality COVID-19 in Two Referral Hospital in Surabaya, Indonesia

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Abstract

Introduction: World Health Organization had identified COVID-19 in January 2019. This disease is caused by SARS-CoV-2, which spread throughout the world and became a pandemic on March 20, 2020. COVID-19 is still a health problem because it has not clear whether the patients will be cured and survive from the disease or not. This study aims to determine the predictors of mortality from COVID-19 at Dr. Soetomo General Academic Hospital and Universitas Airlangga Hospital in Surabaya, Indonesia.

Method: This study was conducted in Dr. Soetomo General Academic Hospital (referral hospital for COVID-19, 1500 beds) and Universitas Airlangga Hospital (Referal Hospital for COVID-19, 600 beds). The study used data on patients with confirmed COVID-19 who were hospitalized at these two referral hospitals. Predictors of mortality were analyzed using logistic regressions.

Result: There were 247 COVID-19 patients enrolled in this study, all patients were tested positive PCR SARS-CoV-2. The main complaints were cough, nasal congestion, dyspnea, and fever. Significant predictor mortality in this study were age >60 years old (OR: 3.24, 95% CI, 1.36 - 7.70), chronic kidney disease (OR: 5.71, 95% CI, 2.05 - 15.89), obesity (OR: 8.22, 95% CI,1.5 - 54.17), malignancy (OR: 6.025, 95% CI, 1.1- 33.00), coronary heart disease (OR: 5.31, 95% CI, 1.28 - 21.98) , and C-reactive protein >10 mg/L (OR 4.603, 95% CI, 2.03 - 10.44).

Conclusions: Obesity and the presence of malignancy, chronic kidney disease, heart disease and age >60 years old are the strongest predictors of mortality in people with COVID-19, despite high CRP results.

Keywords: *Predictors mortality, COVID-19, Indonesia, good health and well-being*

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Background

Coronavirus disease-19 (COVID-19) was identified in December 2019 in the city of Wuhan, China. This disease is caused by Severe Acute Respiratory Coronavirus-2 (SARS-CoV-2). This virus is very contagious, spreading all over the world, and

become pandemic on March 2020.[1] Until now, the problem of morbidity and mortality from COVID-19 has not been resolved properly. The mortality rate for this disease in Indonesia is still high. Based on world meters info on April 21, 2021, there are 43,777 (2.7%) cases of the total cases of 1,614,849. This disease mainly attacked the respiratory system; although it can attack other organ systems, mostly around 80% of symptoms resolve without treatment. However, about 20% of patients will develop serious disease, most notably pneumonia, acute respiratory distress syndrome, sepsis or septic shock, thrombotic stroke and myocardial infarction, and mortality around the world was about 2.1%. [1-4]

The predictor of mortality had not clear yet whether the patient would suffer mild, moderate, or severe disease. Meanwhile, there has not been established proper treatment to overcome the problem of mortality for this disease. Several studies have shown this mortality predictor, including old age and the presence of various comorbid factors such as diabetes mellitus, chronic renal failure, and malignancy. [5,6]

This study aims to determine the predictor of mortality of COVID-19 at Dr. Soetomo General Academic Hospital Surabaya and Airlangga University Hospital Surabaya to improve the case management of COVID-19 as well as predict the prognostic condition of the patient based on existing comorbidities.

Material and Methods

Population and health care setting

The study was conducted in Dr. Soetomo General Academic Hospital (referral hospital for COVID-19, 1500 beds), and Universitas Airlangga Hospital (referral hospital of COVID-19, 600 beds), in Surabaya from April 2020 to June 2020. The study used data on patients with confirmed COVID-19 who were hospitalized at the two referral hospitals.

Study design and inclusion procedure

COVID-19 patients confirmed by PCR who were hospitalized at the Dr. Soetomo General Academic Hospital and Universitas Airlangga Hospital in Surabaya from April 2020 to June 2020 were included in this study. Patients with incomplete data and records were excluded. The study was conducted retrospectively by looking back at the medical records of COVID-19 patients who were hospitalized in the isolation room. Subject characteristic, underlying comorbidities, symptoms, and signs at presentation, laboratory results, the outcome at discharge were collected and evaluated.

Results

There were 247 COVID-19 patients enrolled in this study, age more than 60 years old were 50 (20.2%) patients, female 18(47.7%) patients. The most frequent symptoms were cough 175(70.9%), dyspnea 161 (65.2%), and fever 155 (62.8%), characteristic of the subject can be seen in (Table 1). The most common comorbidities found in these patients were diabetes mellitus, hypertension, and chronic kidney disease.

Table 1 Characteristic of subject study: symptoms of patients on admission

Characteristic Subject	N (%)
Age > 60 y	50 (20.2)
Female	118 (47.7)
Cough	175 (70.9)
Nasal congestion	90 (36.4)
Dyspnea	161 (65.2)
Fever	155 (62.8)
Anosmia	1 (0.29)
Diarrhea	45 (18.2)
Nausea or vomiting	69 (27.9)
Abdominal pain	30 (12.1)

Table 2. Comorbidities associated with the subject

Comorbid conditions	N(%)
Diabetes mellitus	49 (19.8)
Hypertension	41 (16.6)
Chronic kidney disease	25 (10.1)
Malignancy	8 (3.2)
Heart disease	11 (4.5)
Autoimmune diseases	5 (2.0)
Obesity	6 (2.4)
HIV	3(1.2)
Pregnancy	2(0.8)

Table 3. Univariate analysis predictor mortality of COVID-19

	Alive	Deceased	P	Odds Ratio	95% Confidence Interval	
					Lower	Upper
Age > 60 y	36	14	0.006	2.94	1.38	6.26
Female	103	15	0.219	0.71	0.35	1.44
DM	34	15	0.001	3.53	1.66	7.49
Hypertension	28	13	0.002	3.52	1.61	7.71
CKD	14	11	0.000	5.92	2.43	14.41
Obesity	4	2	0.222	2.94	0.52	16.68
Malignancy	5	3	0.102	3.62	0.82	15.839
Autoimmune disease	3	2	0.163	3.94	0.64	24.45
Heart disease	6	5	0.014	5.31	1.53	18.43
Pregnancy	2	0	0.722	0.99	0.99	1.004
HIV	3	0	0.613	0.99	0.97	1.002
CRP >10 mg/L	56	24	0.000	5.08	2.42	10.65
N/L ratio >5.5	82	24	0.003	2.88	1.39	5.98

Table 4. Predictor of Mortality by Binary Logistic Regression analysis

	P	**Odds Ratio**	**95% Confidence Interval**	
			Lower	**Upper**
Age > 60 y	0.008	3.24	1.36	7.70
CKD	0.001	5.71	2.05	15.89
Obesity	0.028	8.22	1.25	54.17
Malignancy	0.038	6.025	1.10	33.00
Heart disease	0.021	5.31	1.28	21.98
CRP >10 mg/L	0.000	4.603	2.03	10.44

Discussion

In this article, we summarized the symptoms and signs most commonly found in COVID-19 cases, namely cough, dyspnea, and fever. In univariate analysis, data was obtained that factors such as age >60 years, female, DM, HT, CKD, obesity, malignancy, autoimmune disease, heart disease, pregnancy, HIV, CRP >10 mg/L, and N/L ratio >5.5 were related to mortality. However, from these factors, age >60 years (p = 0.008), CKD (p = 0.001), obesity (p = 0.028), malignancy (p = 0.038), heart disease (p = 0.02), and CRP >10mg/L (p = 0.000) was statistically significant after being analyzed using logistic regression.

COVID-19 remains the disease-causing world pandemic with a high mortality rate. It is important to know the prognostic factors that play a role in patients with COVID-19.[7] Predicting mortality using pre-existing clinical and laboratory data provides an advantage because it can help stratify the next patient in treatment which then has implications for therapy.[8] The findings of Yang et al.[7] indicated that fever and dyspnea are signs of disease severity.[7] Although our study did not link clinical symptoms with mortality, the findings of this study also found that the majority of these symptoms were found in patients with COVID-19.

Age is an essential factor in the course of the COVID-19 disease. Advanced age is a significant factor in the occurrence of mortality. In a cohort study by Jain et al. of 425 patients, patients aged >65 years had a high risk of mortality, the OR (4.034; 95% CI 1.68–9.71; p=0.002) of in-hospital mortality, but this finding was not that far off in comparison with patients aged >47 years.[6] Research by Estiri et al.[9] also suggests that death occurs in two age groups, namely 45-65 and 65-85. The 45-65 years age group has a high risk of death due to underlying diseases such as DM and mean cancer, while 65-85 years is due to the pulmonary system, including interstitial lung disease, chronic obstructive pulmonary disease, lung cancer, and smoking history.[9] Therefore, age is a prognostic factor for mortality because it is associated with comorbidities in the study population.[6]

A decrease in glomerular filtration rate indicated by an increase in serum urea-creatinine was statistically associated as a predictor of death. Acute kidney injury (AKI) itself is a predictor of mortality in critically ill patients.[10] In the case of COVID-19, data from autopsy shows that the kidney is one of the targets of the SARS-CoV2 virus invasion.[11] The kidney is involved in the pathophysiology of AKI-COVID-19 because the kidneys express angiotensin-converting enzyme 2 (ACE-2) receptors as the entrance to SARS-CoV2 100 times greater than the lung. This mechanism can be a direct cytopathic effect. In addition, immune deposition of viral or viral antigen complexes induced specific immunological effectors also causes kidney damage.[10]

Several cohort-based population studies suggest that obesity is associated with high comorbidities such as DM, HT, and heart disease. The mortality rate is also increased with BMI. Obesity makes patients more susceptible to infection due to a decreased inflammatory cascade. Chronic inflammation in obesity reduces levels of cytokines, adiponectin, leptin and also disturbs the micro-macrovascular response. Lung function is also impaired due to mechanical problems and airway resistance.[12,13]

A single retrospective study by Erdal[14] found the mortality prevalence of cancer-COVID-19 patients to be 23.9%.[14] This figure is relatively high when compared to the general population. This figure is relatively the same as the research in Wuhan, which is around 28.6%. Analysis of the factors associated with the high mortality of the population was an abnormality of inflammatory biomarkers such as low lymphocytes, high CRP, procalcitonin, and D-dimer. The inflammatory response plays an important role in COVID-19, and cytokine storms will cause disease severity [14]. This can occur due to cancer itself or due to chemotherapy.[14]

The latest meta-analysis states that CVD increases the incidence of death in COVID-19 four time-folds.[15] The overactivity of the ACE network contributes to HT and cardiovascular. ACE-2 is associated with cardiac contractility and apoptotic processes due to hypoxia, affecting the outcome of cardiac capacity. In the case of COVID-19 with heart disease, there was an increase in cardiac troponin and an abnormality of electrocardiography by 7.2% and other cardiac biomarkers of 20%.[16]

Markers of inflammation such as lymphopenia have been reported to play a role in the mortality of COVID-19.[8] Although our study did not find a significant association, we found other inflammatory markers that have been widely used in monitoring the progression of COVID-19. C-reactive protein is a valuable marker and gauge of inflammation; it plays an important role in host defense against invading pathogens as well as in inflammation. Early rise in the C-reactive protein also had the strongest association with mechanical ventilation or mortality.[5]

This study has several limitations that need to be studied. First, this study was a retrospective design. Second, we did not perform a subgroup analysis for analysis of prognostic factors for mortality. We also did not analyze the effects of the medication or treatment given to the patients because the standards of care in managing COVID-19 are changing rapidly.

Conclusion

Obesity and the presence of malignancy, chronic kidney disease, heart disease, and age >60 years old are the strongest predictors of mortality in people with COVID-19, besides high CRP results.

Conflict of Interest: All authors state that there are no conflicts of interest.

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Ethical Clearance: The research ethics committee Dr. Soetomo General Academic Hospital and Airlangga University Hospital Surabaya has approved this research (Ref.No:0098/LOF/301.4.2/VIII/2020) and (No: 180/KEP/2020).

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