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Original Article

Risk Factors for Mortality Among Confirmed Covid-19 Patients at RSUP Dr. Kariadi

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Abstract

Background : Coronavirus Disease 2019 (COVID-19) is a communicable disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). On March 11, 2020 the World Health Organization (WHO) declared COVID-19 as pandemic causing mortality in more than 150 countries. China reports the most case is among people aged 30–79 years old and male, meanwhile in Italia the most case is among patients with cardiovascular disease, diabetes, chronic diseases, hypertension, and cancer. This encourages researcher to examine risk factors causing mortality among patients with confirmed COVID-19.
Methods : This is an observational study with multivariate analytical test. The samples involved medical records of died patients with confirmed COVID-19 at RSUP Dr. Kariadi. Risk factors being studied involved age, gender and comorbidities such as hypertension, diabetes, pneumonia, chronic obstructive pulmonary disease (COPD), heart disease, kidney disease, and cancer. Data were analyzed using multiple logistic regression with univariate, bivariate, multivariate, confounding and interaction tests.
Results : An increased risk for mortality was found among confirmed COVID-19 patients aged over 60 years (3.25 times), suffered from hypertension (2.09 times), pneumonia (4.77 times), cancer (11.89 times), heart disease (3.55 times), and kidney disease (5.23 times).
Conclusion : Risk factors involving age, hypertension, pneumonia, cancer, heart disease, and kidney disease increase risk for mortality among patients with confirmed COVID-19. The risk is heightened as patients aged older than 60 years old suffering from pneumonia and cancer simultaneously.

Keywords : Risk factor, Confirmed COVID-19, Mortality

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a communicable disease caused by *Severe Acute Respiratory Syndrome Coronavirus 2* (SARS-CoV-2).[1] On March 11, 2020 the WHO declared COVID-19 as pandemic with increasing number of cases causing death in more than 150 countries.[2,3] Indonesia reported first case of COVID-19 on March 2, 2020 and patient number kept growing.[2] On July 9, 2020 the Ministry of Health reported 70.738 confirmed cases of COVID-19 and 3.417 deaths (Case Fatality Rate/CFR 4.8%) spreading over 34 provinces.[2,3] The COVID-19 task force on February 20, 2021 reported a total of 1.271.353 confirmed cases and 34.316 death rate or 2.7% of the confirmed cases in Indonesia. Central Java was in the third most confirmed cases in Indonesia.[4] The Tanggap COVID-19 of Central Java reported that of 148.819 confirmed cases, 9.306 patients were died.[5] The Siaga Corona of Semarang City reported 30.333 confirmed cases and 2.374 deaths consisting of 1.651 residents of Semarang and 723 non-residents.[6] The Chinese Center of Disease Control (CDC) declared the most case was among people aged 30–79 years old and male, while in Italia the most case was among patients with comorbidities such as heart disease, diabetes, chronic disease, hypertension, and cancer.[7,8]

The death of patients with confirmed COVID-19 was influenced by some risk factors. The association between risk factors and mortality is stronger among older people. People aged over 75 years without additional risk factor have equal risk of those younger than 65 years old.[9] Male has three times higher risk for mortality compared with female.[10,11] Hypertension is the most common comorbidity of COVID-19 with death rate of 58.3%. The second most common comorbidity is diabetes with death rate of 49%. Diabetes and hypertension damage blood vessel structure worsening condition during infections.[12,13] Pneumonia has high fatality rate as lung injury results in lower resistance against viruses and may lead to ARDS.[13] Some studies show that people suffering from COPD have a risk of 1.38 times being infected by COVID-19 compared with those without this condition.[14,15] Respiratory symptoms is the main manifestation of COVID-19, but growing evidences show that it also attacks heart. It was reported that 16.7% and 7.2% COVID-19 patients experience arrhythmia and acute myocardial infarction respectively.[12,13,16] Severe kidney diseases have a great mortality risk, even greater than other comorbidities.[17,18] Since the emergence of COVID-19, cancer patients have a greater risk of being infected and died.[19] For that reason, this study was conducted to examine risk factors such as age, gender, and other comorbidities such as hypertension, diabetes, pneumonia, COPD, heart disease, kidney disease, and cancer which may increase risk for mortality among patients with confirmed cases.

METHODS

This is an observational study with multivariate analytic test. This study recruited samples of medical records of patients died of confirmed COVID-19 having risk factors involving age, gender and comorbidities such as hypertension, diabetes, pneumonia, COPD, heart disease, kidney disease, and cancer at Emergency Room, isolation room and isolation ICU of RSUP Dr. Kariadi. This study excluded patients with probable and suspected COVID-19. Samples were recruited through consecutive sampling. At least 57 medical records meeting inclusion criteria were recruited. The age of medical records was 10 months between March and December 2020.

The data were analyzed with multivariate logistic regression using Excel 2019 and SPSS version 26. Univariate analysis was to describe each independent variable. A bivariate variable selection was conducted between each dependent and independent variable. Once these variables were found to be significant, they were included in the further analysis involving multivariate, confounding, and interaction tests.

This study got ethical approval from research ethic committee of Diponegoro University No.104/EC/KEPK/FK-UNDIP/IV/2021.

RESULTS

This study commenced on May to July 2021 by recruiting samples at Medical Record Department of RSUP Dr. Kariadi. Research samples were recruited consecutively to gather all data within specified period. The secondary data gathered were confirmed cases at RSUP Dr. Kariadi between March and December 2020. There were 184 data meeting inclusion criteria used in the multivariate analysis model encompassing univariate, bivariate, and multivariate analysis.

Data analysis shows 184 confirmed cases involving 95 patients survived (51,6%) and 89 patients died (48,4%) (Table 1).

Risk factors of patients died consist of male 53 patients (49,5%), age over 60 years 32 patients (69,6%), hypertension 38 patients (60,3%), diabetes 28 patients (52,8%), pneumonia 42 patients (73,7%), cancer 10 patients (90,9%), heart disease 12 patients (75%), kidney disease 8 patients (80%), and COPD 2 patients (100%).

Bivariate analysis shows no significant relationship between death risk among patients with confirmed COVID-19 and risk factors including male, diabetes, and COPD so these risk factors do not affect death rate. However, there is a significant association between death rate and risk factors consisting of age over 60 years, hypertension, pneumonia, cancer, heart disease, and kidney disease. Thus, having one or more of these

TABLE 1
Confirmed COVID-19 Patients

Variable	Frequency	%
Death		
Yes	89	48.4
No	95	51.6
Patients died with risk factors		
Male	53	49.5
Age (>60)	32	69.6
Hypertension	38	60.3
Diabetes	28	52.8
Pneumonia	42	73.7
Cancer	10	90.9
Heart disease	12	75
Kidney disease	9	81.8
COPD	2	100

Note: Chi Square Analysis. Significance of p<0.5.

TABLE 2
Bivariat Analysis

Variable	OR (95% CI)	p
Male	1.12 (0.62–2.01)	0.710
Age (>60)	3.25 (1.60–6.63)	0.001
Hipertension	2.09 (1.12–3.90)	0.020
Diabetes	1.28 (0.68–2.43)	0.442
Pneumonia	4.77 (2.39–9.51)	0.000
Cancer	11.89 (1.49–94.98)	0.019
Heart disease	3.55 (1.01–11.44)	0.034
Kidney disease	5.23 (1.09–24.92)	0.038
COPD	$17.64x10^{-11}$ (0)	0.999

Note: Chi Square Analysis. Significance of p<0.5.

risk factors increase death risk among those with confirmed COVID-19. The death risk of patients with confirmed COVID-19 aged over 60 years, and suffered from hypertension, pneumonia, cancer, heart disease and kidney disease increases 3.25, 2.09, 4.77, 11.89, 3.55, and 5.23 times respectively in comparison with confirmed COVID-19 patients survived.

In the multivariate analysis, variables included in the model involved age, hypertension pneumonia, cancer, heart disease, and kidney disease. This model selected risk factors owned by patients with confirmed COVID-19 increasing death risk. The end results show that age, pneumonia, and cancer owned by patients with confirmed COVID-19 simultaneously increase death risk. The confounding test shows that cancer acts as a confounding variable in which cancer risk factor affect death rate among patients with confirmed COVID-19. The interaction test found an interplay between risk factors of pneumonia and age in which death risk increase as they are owned simultaneously.

DISCUSSION

1. General descriptions and increased death risk

The variable of male does not increase death risk different from other study stating that male has greater risk compared with female.[15,20,21] Patients aged over 60 years have a heightened death risk of 3.25 times compared with those aged below 60 years.[20,22] The averaged age of confirmed COVID-19 patients died at RSUP Dr. Kariadi is 57 years. The youngest patient aged 21 years while the oldest patient aged 77 years.

The variable of hypertension increases death risk 2.09 times among confirmed COVID-19 patients. Hypertension commonly experienced by confirmed COVID-19 patients died is type II hypertension. Some patients were suffering from type I hypertension and controlled hypertension but significantly lower than type II hypertension. The variable of diabetes does not increase death risk among patients with confirmed COVID-19 in contrast with previous studies.[13,17,23] The confirmed cases at RSUP Dr. Kariadi were dominated by type II diabetes followed by diabetic ulcer.

The patients with confirmed COVID-19 suffering from pneumonia during clinical investigations have an increased death risk of 4.77 times.[15] The confirmed COVID-19 patients with cancer have a greater death risk of 11,89 time in comparison with those without cancer.[24] Some patients with confirmed COVID-19 died at RSUP Dr. Kariadi suffers from some types of cancer involving *nasofaringeal cancer (malignant neoplasm of nasopharynx), non hodgkin lymphoma (tonsil LNH), medulla spinalis tumour (Multiple Myeloma),* tumor in frontal region, *ovarian cancer, breast cancer*, and *invacive ducral carcinoma*.

The death risk among confirmed COVID-19 patients suffering from heart disease increases 3.55 times.[25,26] The heart disease experienced by confirmed COVID-19 patients died at RSUP Dr. Kariadi involves *congestive heart failure* (CHF), STEMI (ST *elevation myocardial infarction*), NSTEMI (non-ST *elevation myocardial infarction*), *coronary artery disease* (CAD), and *supraventricular tachycardia* (SVT). The death risk of patients with confirmed COVID-19 suffering from kidney disease increases 5.23 times.[27] Types of kidney

disease among confirmed COVID-19 patients include *chronic kidney disease* (CKD), *acute kidney injury* (AKI) and azotemia. Some CKD patients underwent dialysis therapy. No increased death risk was found among those with confirmed COVID-19 and COPD.[28,29] The type of COPD experienced by confirmed COVID-19 patients is emphysema.

2. The association between risk factors and mortality

RSUP Dr. Kariadi is a referral hospital for COVID-19 providing care to 727 confirmed cases in 2020. Of the many cases, the percentage of male patients died was 49.5% lower than that of female patients. This finding is in accordance with a study conducted by Dehingia N showing that the percentage of female patients died was higher than that of male patients which occurred in India, Vietnam, Nepal and Slovenia.[30] However, a study conducted by Jim JM, *et al.* shows different findings as generally male has higher risk related to biological and habitual factors than female does.[21] The biological factors involve immune response and habit such as smoking. These differences may occur as a result of incomplete data, geography, biased data identification, or countries with high risk of women's health issues.[21]

Patients aged above 60 years have a high death rate of 69,6%. This finding is in line with a study conducted by Indarwati R stating that this may be caused by factors such as comorbidity or lowered immune system. Psychological factors also play an important role as limitation of social interaction lowers mental health.[22] The limitation of social interaction experienced by elderly involves limitation of participation in Posyandu Lansia. Posyandu lansia is a place where elderly gathers with peers so they do not feel lonely.[22]

There is an association between COVID-19 and hypertension worsening patient's conditions. During this study, 60.3% patients died was found to have hypertension. This finding is corroborated by a study by Du Y, *et al.* stating that SARS-CoV-2 viruses possess ACE 2 receptors. Anti-hypertensive drugs acting as ACE inhibitor increase the number of ACE 2 receptors on cell surface. For that reason, patients consuming anti-hypertensive drugs experience more severe infection which may lead to death.[31] In addition, a study by Yustinawati R and Achadi explains that death may occurs as level of ACE 2 drastically drop even before immune systems are able to control virus population.[20]

A meta-analysis by Corona G, *et al.* indicates that COVID-19 patients suffering from diabetes possess death risk twice higher than those without diabetes. There is no specified explanation related to the causes of this elevated mortality, but some factors may be responsible such as lung dysfunction related to decreased lung volume, lung diffusion capacity, ventilation control, and bronchomotor tone. Prognosis may be compromised as patients suffer from hyperglycemia. Besides, diabetic patients are more susceptible for infections.[32] However, this study contradicts these findings as patients suffering from confirmed COVID-19 and diabetes simultaneously died at RSUP Dr. Kariadi (52.8%) do not have an increased death risk.

A high number of patients with confirmed case and pneumonia died at RSUP Dr. Kariadi (73.7%). This finding is in line with a study conducted by Hidayani WR explaining that mortality may be caused by symptoms such as fever, tachypnea (≥ 30x/minutes), dyspnea, and low saturated oxygen.[15] Another study conducted by Elezkurtaj, *et al*. elucidates that purulent pneumonia with and without abscess found on died patients during an autopsy was most numerous in comparison with other risk factors being studied.[26]

A study conducted in Norway by Johannesen TB, *et al.* comparing cancer and non-cancer patients found no significant increase of death risk of confirmed COVID-19 patients suffering from overall cancer, but an increased death risk was found among those suffering from metastatic cancer.[24] In other hand, the death rate of cancer patients at RSUP Dr. Kariadi was 90,9% which is in line with a study conducted in China by Zhou Y, *et al*. in which the death rate of confirmed COVID-19 patients was 11.7% higher than those without cancer. The most commonly cancer is lung cancer followed by breast cancer and rectal cancer.[33]

In this study, the death rate of patients suffering from heart disease was 75%. This finding is in accordance with previous study by Harrison SL and Cordero A, *et al.* claiming that there was an increase of death rate of confirmed COVID-19 patients suffering from heart disease. It was caused by pro-inflammatory response related to upper respiratory tract infection, immune dysregulation worsening susceptibility and severity, smoking and obesity among heart disease patients.[23,34]

The patients with confirmed COVID-19 suffering from kidney disease died at RSUP Dr. Kariadi was 80%. A study conducted by Drew C, *et al.* explained that COVID-19 impairs cell membrane permeability through inflammatory cytokine and antigen-antibody complex formation.[35] A study conducted in Italia by Gibertoni D, *et al.* found that majority of confirmed COVID-19 patients suffering from kidney disease is old and had multiple comorbidities. The death rate of patients suffering from kidney disease are higher than those without kidney disease as this condition had chronically affected kidney.[27]

A study conducted by Lee SC, *et al*. found that COPD worsens clinical outcomes as poor lung function. COPD is a heterogenous disease with various severity levels, exacerbation frequency, and comorbidities.[29] Gerayeli FV, *et al*. claimed that confirmed COVID-19 patients suffering from COPD owned a high death risk which may be caused by an increased ACE 2 receptors in

respiratory tract and lung. COPD is also tightly related to impaired immune sistem.[28] In comparison with previous two researches, this study did not find an increase of death risk.

3. Research limitations

This study has limitations. The medical records being analyzed was only 184 of 727 as some medical records could not be found, data was mixed with other variables, and incomplete data. Besides, the proposed period of study was between March and December, however the diagnose of confirmed COVID-19 was adopted since July so the study period was altered.

There is inaccuracy in processing data which may lead to bias. The definition of heart disease, kidney disease, and COPD had not been specified so it had broad meaning. Other risk factors found during study did not included as risk factors.

CONCLUSION

The conclusions of this study are some risk factors involving age, hypertension, pneumonia, cancer, heart disease, and kidney disease increase death risk among patients with COVID-19 patients. Patients aged over 60 years suffering from pneumonia and cancer simultaneously possess higher death risk. Gender, diabetes and COPD do not increase death risk.

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