



Factors Influencing The Duration Of Illness to Mortality In Confirmed COVID-19 Patients Admitted to Hospitals Across Riau Province

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Received : 13-07-2023

Accepted : 10-08-2023

Published : 17-09-2023

ABSTRACT

This study aims to look at the factors associated with the length of illness to death in COVID-19 patients being treated in hospitals throughout Riau Province. Researchers used secondary data sourced from data from the Online Hospital at the Riau Provincial Health Office. The overall cumulative survival probability for dying was 6.2%, with an overall median survival time of 20 days (IQR: 17-22). The lowest median survival time is the initial saturation value variable, which is 4 days (IQR: 2-5), the use of a respirator is 5 days (IQR: 3-6), and ICU care is 8 days (95% CI: 8-9). The final results of multivariate analysis showed that old age had a 1.7 times risk of experiencing death HR 1.747 (95% CI: 1.386-2.202), a low initial saturation value had a 1.6 times risk of experiencing death HR 1.627 (95% CI: 1.155-2.292), care units in the ICU have a 1.9 times risk of dying with HR 1.911 (95% CI: 1.439-2.538) and patients who use respirators have a 1.4 times risk of dying with HR values 1.463 (95% CI: 1.051-2.037). Improvement and readiness of referral health facilities in Riau Province is something that deserves attention as a preventive effort in facing the possibility of the next emerging disease.

Keywords: covid-19, survival, riau, hospital.

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INTRODUCTION

The COVID-19 case in Indonesia was first discovered in Depok, West Java, and was officially announced on March 2 (Ministry of Health, 2019). The spread of the virus, which has a single-stranded RNA (single-stranded RNA) called the SARS Cov-2 virus, is taking place quickly throughout Indonesia, causing considerable death in the community. Deaths from COVID-19 in Indonesia are the second highest in Asia and the largest in Southeast Asia. According to data released by WHO as of February 28, 2023, there were 160,914 deaths out of 6,736,046 confirmed cases throughout Indonesia (Covid-19.who.int, 2023).

Riau Province is one of the provinces on the island of Sumatra which is located on a strategic route and is directly adjacent to the Provinces of North Sumatra, West Sumatra Province, Jambi Province, and the Riau Archipelago Province and is directly facing 2 (two) neighboring countries, namely Malaysia and Singapore. After 3 years of the COVID-19 pandemic, Riau Province is the area with the largest number of confirmed cases on the island of Sumatra. According to the Riau Province COVID-19 daily report, as of March 29, 2023, there were 154,586 confirmed cases of COVID-19 with 4549 deaths (COVID-19, 2022).

The risk factors for COVID-19 death consist of several aspects, such as sociodemographic, clinical, and care factors received by patients. Most studies on COVID-19 in the world and in Indonesia state that age plays an important role in a person's survival when infected with the SARS-CoV-2 virus, where more deaths occur in the elderly. Research in DKI Jakarta Province conducted to look at the risk factors for death in COVID-19 patients stated that elderly patients and patients with co-morbidities or co-morbidities dominated the risk factors for death. (Surendra et al., 2021).

Literature studies from review articles conducted at the start of the pandemic stated that COVID-19 patients with co-morbid hypertension, obesity, chronic lung disease, diabetes, and cardiovascular disease had a poor prognosis and were at great risk of experiencing Acute Respiratory Disorder Syndrome (ARDS) and pneumonia. Which can increase the risk of death (Rahayu et al., 2021). Older patients, especially those aged 65 and over with co-morbidities and infected with COVID-19, have an increased rate of intensive care (ICU) and death from COVID-19 disease (Sanyaolu et al., 2020) ; (Sattar et al., 2020). Other studies also state that the increased risk of death is closely related to the elderly, gender, and smoking history (Ernawati, 2021). In addition, patients who have a history of co-morbidities such as diabetes, cerebrovascular disease, COPD, hypertension, acute kidney failure, and cancer greatly affect the risk of death in COVID-19 patients (Albitar et al., 2020) ; (de Almeida-Pititto et al., 2020) ; (Dessie & Zewotir, 2021).

This study aims to determine the factors associated with the length of illness to death in patients with confirmed COVID-19 in hospitals throughout the Riau Province in 2022. This research can provide additional information and input material for policymakers in Indonesia, especially the Department of Health Riau Province, to evaluate implementing the COVID-19 countermeasures program.

METHODS

This research is an analytic observational study with a retrospective cohort design using secondary data taken entirely as a sample (total sampling). The inclusion criteria in this study were confirmed cases of COVID-19 who died in hospital in 2022; cases were residents of Riau Province and reported in RS Online data. Exclusion criteria were samples that did not have data on the length of time they were sick until they were reported dead/recovered (time to event) or incomplete variable data. The time of onset of illness is calculated from the time the case gets the first positive result at the time of the PCR swab examination (confirmation) and is admitted to the hospital; the time of death/recovery is the date when the patient leaves the hospital with the status of death/recovery. The events in this study were patients with death status at the end of treatment, while the sensors were patients with recovery status at the end of treatment. Age was divided into 3 categories, namely <40 years, 40-60 years, and >60 years. Initial saturation values are categorized into low saturation values (<93%) and high $\geq 93\%$. The severity level is divided into 2 categories: asymptomatic + mild and moderate + severe. Co-morbid history is a patient with co-morbid conditions at hospitalization, such as hypertension, diabetes mellitus, cardiovascular disease, cancer, COPD, and other diseases. A breathing apparatus is a ventilator or ECMO device installed and used when the patient is hospitalized. Figure 1 shows the flow of sampling in this study. Of the 1382 people treated at the Riau Provincial Hospital from January 1 to December 31, 2022, there were 74 residents outside the Riau Province, 20 people outside the study period, and 76 people did not have complete dependent data. Of these, 1212 people were taken as samples according to predetermined inclusion and exclusion criteria. This research was conducted at the Riau Provincial Health Office in May 2023. This research received approval from the Research Ethics and Community Service Commission, Faculty of Public Health, University of Indonesia with Number: Ket-392/UN2.F10.D11/PPM.00.02/2023. Kaplan Meier and Cox Regression analysis was carried out to look at the cumulative survival probability, median survival time, and Hazard Ratio of the variables/factors that are considered to be related to COVID-19 deaths in Riau Province. Data were analyzed using IBM SPSS Version 25.

RESULTS AND DISCUSSION

Based on data from the Online Hospital report, there were 1382 confirmed cases of COVID-19 who were treated at the Riau Province Hospital from January 1 to December 31, 2022. Of these, 1212

people were taken as samples according to predetermined inclusion and exclusion criteria. The flow of research sampling can be seen in the chart as follows:

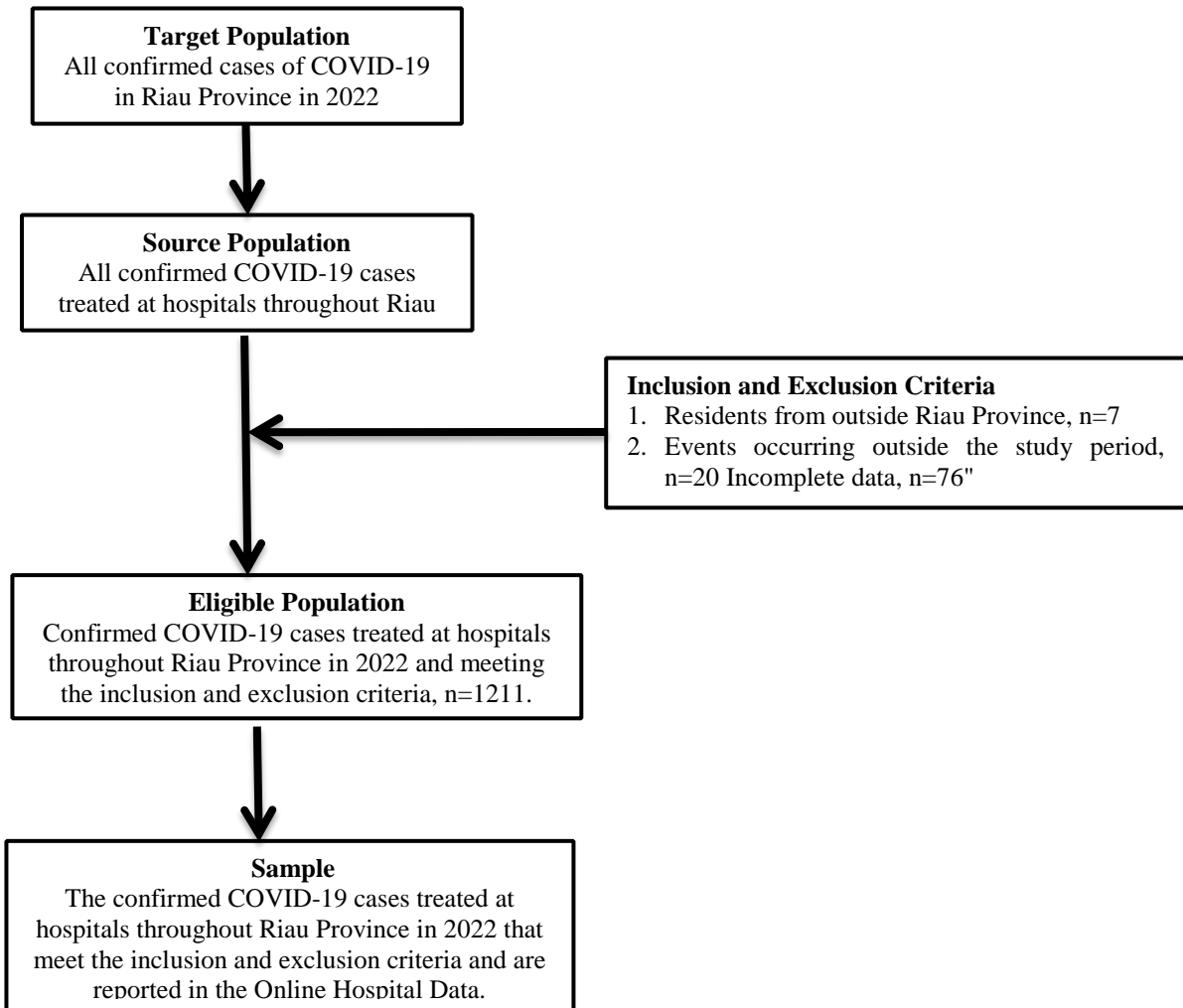


Figure 1. The flow of Research Sampling

Table 1. Kaplan Meier Analysis Based on Survival Status

Variable	Events n=317	sensors n=895	S(t)	P-values	Median Survival Time
Overalls (Overall)			0.062		20 (17-22)
Age				<0.001	
≤ 40 years	43 (9,2)	426 (90.8)	0.384		29 (9-48)
41-60 years	107 (28.8)	264 (71.2)	0.182		20 (13-26)
> 60 years	167 (44.9)	205 (55.1)	0.116		11 (8-13)
Type Sex				0.013	
Woman	144 (22.4)	500 (77.6)	0.193		20 (14-25)
Man	173 (30.5)	395 (69.5)	0.075		18 (15-20)
Initial Saturation				<0.001	
≥ 93% (High)	240 (21.6)	871 (78.4)	0.094		22 (17-26)
< 93% (Low)	101 (76.2)	24 (23.8)	0.038		4 (2-5)
Severity Level					
Asymptomatic + Mild	127 (18.6)	557 (81.4)	0.569	<0.001	29
Medium + Heavy	190 (36.0)	338 (64.0)	0.046		14 (11-16)
Oxygen Therapy				<0.001	
No	127 (18.6)	557 (81.4)	0.569		29

Variable	Events n=317	sensors n=895	S(t)	P-values	Median Survival Time
Yes	190 (36.0)	338(64.0)	0.046		14 (11-16)
Co-morbid history				<0.001	
No	247 (23,3)	814 (76.7)	0.155		20 (16-23)
Yes	70 (46.4)	81 (53.6)	0.055		11 (7-14)
Treatment Place				<0.001	
Non-ICU	160 (16.9)	787 (83.1)	0.546		29
ICU	157 (59.2)	108 (40.8)	0.049		8 (6-9)
Respiratory Apparatus				<0.001	
Not installed	247 (26.0)	874 (74.0)	0.075		20 (16-23)
Installed	91 (76.9)	21 (23.1)	0.057		5 (3-6)

Of 1212 confirmed COVID-19 patients treated at hospitals throughout Riau Province, there were 895 people (73.8%) who experienced recovery/survived at the end of treatment (sensor) and 317 people (26.2%) who died (event) at the end of treatment. Based on patient characteristics, the majority of patients who died were >60 years old (44.9%), male (30.5%), had an initial saturation value of <93% at the time of admission (76.2%), had a history of co-morbidities (46.4%) and had moderate + severe severity (36%) Based on the care received at the hospital, there were 18.6% of patients who experienced an event did not get oxygen therapy, 59.2% of patients who died were treated in the ICU and 76.9% of 112 patients wearing respirators had an event at the end of their stay.

Table 1 shows that the overall cumulative survival probability from illness to death in patients treated at hospitals throughout Riau Province was 0.062 (6.2%), with a median survival time of 20 days (IQR: 17-22). The lowest probability of survival was in patients with a low initial saturation value of <93%, namely 0.038, followed by moderate/severe severity, namely 0.046, and treatment in the ICU, namely 0.049. The lowest median survival time was in patients with low initial saturation values, namely 4 days (IQR: 2-5), and patients using respirators, namely 5 days (IQR: 3-6). There is a difference in the cumulative survival probability in terms of age, where patients aged >60 years have a lower probability of 0.116 (11.6%) compared to patients aged <40 years, namely 0.384 (38.4%). The probability of experiencing death was also lower in the male sex (0.075), history of co-morbidities (0.055), place of care (0.049), and use of respirators (0.057).

From the results of the log-rank test, it can be seen that all the variables studied have a p-value <0.05. Based on these results, there is a difference in the cumulative survival probability based on the category for each factor which is significant and statistically significant.

Table 2. Bivariate and Multivariate Analysis of Related Factors With Length of Sickness Up to Death of COVID-19 Patients at Riau Province Hospital

Variable	Crude Hazard Ratio (95% CI)	P-values	Hazard Ratio (95%CI)	P-values
Age				
≤ 60 years	ref			
> 60 years	2.36 (1.89-2.95)	<0.001	1,747 (1,386-2,202)	<0.001
Type Sex				
Woman	ref			
Man	1.31 (1.05-1.64)	<0.015	1.175 (0.938-1.472)	0.160
Initial Saturation				
≥ 93 % (high)	ref			
< 93 % (low)	3.83 (2.96-4.97)	<0.001	1,627 (1,115-2,292)	0.005
Severity Level				
Asymptomatic + Mild	ref			
Moderate + Heavy	1.80 (1.43-2.26)	<0.001	1.174 (0.903-1.646)	0.230
Co-morbid history				
There aren't any	ref			

Variable	Crude Hazard Ratio (95% CI)	P-values	Hazard Ratio (95%CI)	P-values
There is Oxygen Therapy	1.81 (1.38-2.37)	<0.001	1.231 (0.921-1.646)	0.160
Yes	ref			
No	1.80 (1.43-2.26)	<0.001	1.174 (0.903-1.646)	0.230
Treatment Place				
Non-ICU	ref			
ICU	3.12 (2.50-3.91)	<0.001	1,911 (1,439-2,538)	<0.001
Use of Tools				
Not installed	ref			
Installed	3.41 (2.61-4.46)	<0.001	1,463 (1,051-2,037)	0.024

Before conducting the Cox regression analysis, we statistically evaluated *the goodness of fit* to assess whether the variables studied were satisfactory assumption *proportional hazard* (PH). From the analysis results, no variables violate the PH assumption because all variables have a $p > 0.05$, so they can proceed to the next analysis. Based on Table 2, it can be seen that the highest *Crude Hazard Ratio to death in confirmed cases of COVID-19 is in the initial saturation variable with a CHR value of 3.83 (2.96-4.97) and in the variable use of respiratory aids with a CHR value 3.41 (95% CI 2.61-4.46)*. The results of the Cox regression analysis also stated that all the factors studied had a statistically significant relationship with a p -value < 0.05 . Patients aged > 60 had a risk of dying 2.36 times (95% CI 1.89-2.95) greater than patients aged < 60 . The male gender has the opportunity to die 1.3 times (1.05-1.64) compared to patients with the female gender. Patients with an initial saturation value of $< 93\%$ had a 3.83 times risk of dying, and patients with moderate and severe severity had a 1.8 times risk (95% CI 1.43-2.26) of dying. In the co-morbid history variable, patients with a co-morbid history are 1.8 times more likely to die from COVID-19. While patients treated in the ICU have a 3 times greater risk of dying than those treated in other rooms. Patients who receive oxygen therapy also have a 1.8 times greater chance of dying than those who do not receive oxygen. Meanwhile, patients who use respirators have a 3-fold greater risk of dying than those who do not (table 2). The final results of a multivariate analysis of factors related to the length of illness to death in COVID-19 patients treated at the Riau provincial hospital show that old age has a 1.7 times risk of dying HR 1.747 (95% CI: 1.386-2.202), low initial saturation values have a 1.6 times risk of dying HR 1.627 (95% CI: 1.155-2.292), care settings in the ICU have a 1.9 times risk of dying with HR 1.911 (95% CI: 1.439 -2.538) and patients who use respirators have a 1.4 times risk of dying with an HR value of 1.463 (95% CI: 1.051-2.037).

The median survival time for experiencing death in Riau Province is 20 days (IQR: 17-22). Research conducted by Thai on the survival of COVID-19 patients in Vietnamese hospitals showed that the median survival results were not much different, namely 21 days (IQR: 16-34) (Thai et al., 2020). Cases of COVID-19 death at the Riau Province Hospital were more common in women (53.1%), but the cumulative survival probability for experiencing death was lower in males (0.075). These results align with research in East Jakarta from March to September 2020, which stated that the mortality rate for confirmed COVID-19 patients was 2.53%, with the majority of cases being female (52.31%). A study conducted in DKI Jakarta at the start of the pandemic on factors related to COVID-19 deaths stated that most deaths occurred at an older age (Drew & Adisasmita, 2021). Research conducted in Brazil and Italy also stated that old age is a risk factor for death from COVID-19, where the elderly group in Brazil has a 3.7 times higher risk than the younger group (Rozaliyani et al., 2020). Boys and girls have the same probability of suffering And infected C COVID-19 (Sousa et al., 2020); (Grasselli et al., 2020). In older age COVID-19 patients, an *inflammation process occurs*, i.e., disruption of the innate and adaptive immune systems associated with the production of cytokine And mediator inflammation, Which triggers storm cytokine that causes ARDS and multi-organ failure,

which is at risk of death. High mobility in the community occurred during regional head elections in several provinces and districts/cities in Indonesia at the end of 2020 and the implementation of joint leave during the Eid al-Fitr celebration in May 2021 (Perrotta et al., 2020). This phenomenon also occurred in Riau Province, where there were 9 regencies/cities that held simultaneous regional head elections on December 9, 2020, and it is customary for the people in Riau to keep in contact during religious holiday celebrations even during the COVID-19 pandemic situation (Sukirmana et al. . . , 2022).

Research conducted in one of the hospitals in Indonesia states that there is a difference in the probability of survival of death in co-morbid history with a value of $p = <0.001$ (Hartantri et al., 2023). A retrospective cohort study on risk factors for COVID-19 conducted in Ethiopia also showed statistically significant differences in the probability of survival in the co-morbid history status variable with a p -value = <0.001 (Hartantri et al., 2023). Although not statistically significant in the multivariate final model, co-morbid factors can be considered to have contributed to the increase in COVID-19 mortality in Riau Province. Based on NAR data from Riau Province, the largest co-morbid reported cases of COVID-19 death was Diabetes Mellitus (26.5%). Four studies report that the case fatality rate for COVID-19 is three times higher in people with diabetes compared to those without diabetes (2.3% vs. 7.3%) (Wu et al., 2020). kindly global prevalence of diabetes in the year 2019 is estimated to big 9.3% and is expected to increase become 10.2% in the year 2030 And 10.9% in the year 2045 (Saeedi et al., 2019). The high prevalence of diabetes in the general population causes diabetes to become a disease accompaniment the second after hypertension in a patient with COVID-19 (Bajgain et al., 2020) ; (Rahayu et al., 2021). Complications caused by diabetes can increase the risk of death in patients with COVID-19, where there is a direct increase in glucose levels, which increases the replication of SARS-CoV-2. This mechanism of g- glycolysis will maintain the replication of SARS-CoV-2 by producing *mitochondriareactive oxygen species* (ROS) and activating *hypoxia-inducible* factor (HIF) 1 α and support the occurrence of proliferation viruses (Lim et al., 2021). The results of this study are in line with research conducted in Ceara, Brazil, which states that there are differences probability of survival for patients with COVID-19 with a history of type 2 DM compared to patients who do not have type 2 DM with the results of the log-rank test, namely $p = <0.001$ (Sousa et al., 2020). The low resilience life patient COVID-19 who has a history of diabetes This closely related to the system immune And response inflammation in patients, which causes the condition to become more severe and leads to death (Fleming et al., 2021) ; (Gupta et al., 2021).

Another factor related to the death of COVID-19 patients is the management and care that patients receive at the hospital. Most COVID-19 patients have mild or asymptomatic symptoms, and only a small proportion experience severe or critical levels of severity. The initial saturation value greatly affects the severity experienced by COVID-19 patients. About 14% of patients who show severity need to use a ventilator, And around 5% require treatment in ICU for the amount needed mechanical ventilation. A meta-analysis of 45 studies looking at risk factors for COVID-19 requiring ICU care stated that the average time needed for patients to be treated in ICU was 10.8 days (95% CI: 9.3-18.4) (Tan et al., 2021). Research conducted in England describes the percentage of DRILL rooms caring for ventilatedpatients related to the risk of death from COVID-19. Results studies state that a high percentage of BOR (85-100%) has a risk of 1.2 times (95% CI: 1.06 – 1,4) compared to reference Lower BOR (45-85%). In low BOR conditions (0-45%), the risk is 0.82 (95% CI: 0.73-0.93) and becomes a factor protective against COVID-19 death (Wilde et al., 2021).

This study has limitations because the cumulative survival probability and hazard ratio values of the variables measured are general values. After all, the data used is on all COVID-19 patients who died and were treated at all hospitals in Riau Province. Each hospital, of course, has different facilities, infrastructure, and human resources. So that with different conditions between hospitals, it can provide

different results of treatment and survival for COVID-19 patients undergoing treatment. The COVID-19 pandemic has had an extraordinary impact on system changes in service health in Indonesia. The need for very high health services occurred at a time when an increase in COVID-19 cases occurred in all regions. The impact felt is that health facilities cannot accommodate many patients who need treatment. Each country, including local governments in Indonesia, has diverse capabilities in providing health facilities and providing health services during the COVID-19 pandemic. This is one of the causes of differences in survival, primarily on the ability to increase the amount of place Sleep at home Sick, specifically in the ICU, And public health policy to address the pandemic. Research with samples and hospital locations of the same type is needed to determine how big the Hazard Ratio is from factors related to death in confirmed COVID-19 patients in Riau Province (Tan et al., 2021). However, the results of this study can be used as a reference and additional information for the Riau Provincial Health Office to improve health service efforts, especially the prevention of co-morbidities and improvement of referral health facility services in Riau Province.

CONCLUSION

The majority of the cumulative survival probability and median survival time for COVID-19 deaths are lower in patients >60 years of age, male sex, have a history of co-morbidities, low initial saturation values in hospital, moderate+low severity and undergoing treatment at ICU and using a respirator. The results of the multivariate analysis showed a statistically significant relationship for all variables with a p-value <0.05. Factors that have a significant relationship with the survival of COVID-19 patients treated at Riau Provincial Hospital are age, saturation factor at initial admission, place of care, and use of breathing apparatus. Improvement and readiness of referral health facilities in Riau Province deserve attention as a preventive effort in facing the possibility of the next emerging disease. In addition, efforts to prevent diseases that have the potential to become co-morbid need to be increased because they have a large risk of death from COVID-19 and the co-morbid disease itself.

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