Mortality Risk Factors of COVID-19 Inpatients at Panembahan Senopati Hospital, Bantul, Yogyakarta

Christiana Sri Wahyuningsih[1], Esthi Budhi Asih[1],
Ledy Vinantika[2], Ria Sulistiani[2]

[1]Nursing and Quality Assurance, Panembahan Senopati Hospital, Bantul, Yogyakarta
[2]Reporting Unit, Panembahan Senopati Hospital, Bantul, Yogyakarta

ABSTRACT

Background: COVID-19 Case Fatality Rate (CFR) in Bantul district is 2.64%. This figure is higher than the world CFR reported by WHO of 2.07%. Panembahan Senopati Regional General Hospital is a hospital owned by the Regional Government of Bantul Regency and is one of the COVID-19 referral hospitals. This study aims to determine the characteristics and risk factors for the death of inpatient COVID-19 patients at Panembahan Senopati Hospital.

Subjects and Method: This type of study is observational analytic with a retrospective cross-sectional design. This research was carried out from July to September 2021 at Panembahan Senopati Hospital. A total of 289 research subjects were selected in total sampling. The dependent variable is the mortality of COVID-19 patients. The independent variables were age, sex, diabetes mellitus, hypertension, chronic renal failure, heart disease, immunological disorders, and chronic liver failure. The data were analyzed by multiple logistic regression.

Results: Risk factors for death in hospitalized COVID-19 patients were age, diabetes mellitus, hypertension, and chronic renal failure. Age ≥60 years was 2.13 times more likely to cause death (OR = 2.13; CI 95% = 1.24 to 3.66; p=0.006). Hospitalized COVID-19 patients with comorbid diabetes Mellitus were 2.31 times more likely to cause death (OR= 2.31; CI 95% =1.30 to 4.12; p=0.004). Hospitalized Covid-19 patients with comorbid hypertension 2.18 times chance of causing death (OR= 2.18; CI95% =1.12 to 4.25; p= 0.021). Hospitalized COVID-19 patients with comorbid chronic renal failure were likely to cause 3.25 times the death rate (OR= 3.25; CI 95%= 1.11 to 9.51; p=0.031).

Conclusion: Risk factors for death in hospitalized COVID-19 patients are age, diabetes mellitus, hypertension, and chronic renal failure.

Keywords: Hospitalization, death, COVID-19 patients

Correspondence:
Christiana Sri Wahyuningsih. Nursing and Quality Assurance, Panembahan Senopati Hospital. Jl. Dr. Wahidin Sudiro Husodo, Trirenggo, Bantul, Yogyakarta. Email: anachristi19@gmail.com. Mobile: +6281287783924.

BACKGROUND

Coronavirus Disease 2019 (COVID-19) is a new type of zoonotic disease that has never been identified before in humans. This disease is an emerging infectious disease (EIDs). EIDs are diseases that appear and

attack a population for the first time, or have existed before but increase very quickly, either in terms of the number of new cases in a population or spread to new geographical areas (Ministry of Health, 2021b). This outbreak of an unknown pneumonia virus of unknown etiology was first introduced in Wuhan, China on December 12, 2019. The virus that causes COVID-19 is called Sars CoV-2 (Severe acute respiratory syndrome Coronavirus (Ji et al., 2020). Common signs and symptoms of COVID-19 infection include symptoms of acute respiratory distress such as fever, cough, and shortness of breath. The average incubation period is 5 to 6 days with the longest incubation period being 14 days. In severe cases of Covid-19, it can cause pneumonia, acute respiratory syndrome, kidney failure, and even death (Ministry of Health, 2020).

On January 30, 2020, WHO designed COVID-19 as a Public Health Emergency of International Concern (KKMMD / PHEIC), and on March 11, 2020, was designated as a pandemic because the transmission of this virus is very fast and occurs between countries (Mona, 2020). As of August 30, 2021, a total of 216,303,376 confirmed cases were reported with 4,498,451 deaths (CFR= 2.0%) worldwide. A total of 41,178,198 are confirmed cases from Southeast Asia (WHO, 2021).

COVID-19 was first reported in Indonesia on March 2, 2021, with 2 cases (Ministry of Health, 2020). Until now, cases have been increasing and spread throughout Indonesia. The total confirmed cases of COVID-19 in Indonesia as of August 30, 2021, were 4,079,267 with 132,491 cases of death (CFR= 3.4%) (Ministry of Health, 2021b). In DIY, based on the report of the District/City Health Office and Covid-19 Referral Hospital as of August 30, 2021, the number of patients confirmed positive for COVID-19 was 149,379 people with 4,816

cases of death (CFR= 3.2%) (DIY Health Office, 2021). A total of 54,416 of them were positive confirmed cases from Bantul Regency with 1,437 death cases (CFR= 2.6%) (Dinkes Bantul, 2021).

Old age is said to be associated with the risk of death in Covid-19 patients (Rozaliyani et al., 2020). The age of ≥60 years increases the risk of death from Covid-19 by 2.17 times and the age of >64 years has a 2.09 times chance of dying from Covid-19 compared to the age of ≤64 years (Satria et al., 2020). Cases of death of the elderly with COVID-19 are dominated by male patients (Azwar et al., 2020). Male gender is one of the risk factors for death in COVID-19 patients (Satria et al., 2020). Men increased mortality RR by 2.15 times (Drew and Adisasmita, 2021). Male confirmed cases are 7.22 times more likely to die from Covid compared to female confirmed patients (OR= 7.22) (Wang et al., 2020)

The presence of comorbid diseases is also a risk factor for death in COVID-19 confirmed patients. Hypertension is said to be associated with the risk of death (OR= 1.86). Chronic renal failure (RR= 3.33), hypertension (RR= 2.45), and respiratory tract symptoms (RR= 2.17) are risk factors for death in Covid-19 patients (Drew and Adisasmita, 2021). Comorbid Diabetes Mellitus (DM) in Covid-19 patients is also 4.34 times more likely to cause death compared to those who are not comorbid DM (Satria et al., 2020). The Covid-19 Case Fatality Rate (CFR) in Bantul district is 2.6%. This figure is higher than the world CFR reported by WHO of 2.0%.

Panembahan Senopati Regional General Hospital is a hospital owned by the Regional Government of Bantul Regency and is one of the Covid-19 disease referral hospitals based on a decree from the Ministry of Health No.HK.01.07-MENKES- 169-2020 concerning the Determination of

Referral Hospitals for the Management of Certain Emerging Infectious Diseases.Therefore, researchers want to explore the characteristics and risk factors for death in inpatient Covid-19 patients at Panembahan Senopati Hospital Bantul.

SUBJECTS AND METHOD

1. Study Design
This study is an observational analytical study using a retrospective research design. This study was conducted at Panembahan Senopati Bantul Hospital which was carried out from January to August 2021.

2. Population and Sample
The source population in this study is COVID-19 patients who were hospitalized in July 2021 at Panembahan Senopati Hospital Bantul. Sampling was selected in total as many as 289 research subjects.

3. Study Variables
Variables included in this study were infection, testing, prevention, masks, and vaccination.

4. Operational Definition of Variables
The death of COVID-19 patients: is COVID-19 patients who were previously hospitalized and declared dead by the doctor in charge.

Age: is the age of hospitalized COVID-19 patients calculated based on the year of birth.

Sex: is a physically and biologically differentiated gender status in hospitalized COVID-19 patients.

Diabetes mellitus: is a history of diabetes mellitus in hospitalized COVID-19 patients diagnosed by doctors and listed in medical records in accordance with the International Statistical of Disease and Related Health Problems-10 (ICD-10).

Hypertension: a history of hypertension in hospitalized COVID-19 patients diagnosed by doctors and listed in medical records in accordance with the International

Statistical of Disease and Related Health Problems-10 (ICD-10).

Chronic kidney failure: a history of chronic kidney failure in hospitalized COVID-19 patients diagnosed by doctors and listed in medical records in accordance with the International Statistical of Disease and Related Health Problems-10 (ICD-10).

Heart Disease: is a history of chronic kidney failure in hospitalized COVID-19 patients diagnosed by doctors and listed in medical records in accordance with the International Statistical of Disease and Related Health Problems-10 (ICD-10).

Immunological disorders: are a history of immunological disorders in hospitalized COVID-19 patients diagnosed by doctors and listed in medical records in accordance with the International Statistical of Disease and Related Health Problems-10 (ICD-10).

Chronic liver failure: is a history of chronic liver failure in hospitalized COVID-19 patients diagnosed by doctors and listed in medical records in accordance with the International Statistical of Disease and Related Health Problems-10 (ICD-10).

5. Study Instruments
The research instrument used for data collection is secondary data obtained from the Surveillance and KLB Information System (SISKLB) of Bantul Regency.

6. Data Analysis
Univariate analysis to obtain the frequency distribution and percentage characteristics of the study subjects. Bivariate analysis to analyze the relationship between independent and dependent variables uses the Chi-Square test and the Odds Ratio (OR) with a CI 95% and a significance level of $p<0.050$. Multivariate analysis using multiple logistic regression analysis.

RESULTS
Univariate analysis to obtain the frequency distribution and percentage characteristics

of the study subjects. Bivariate analysis to analyze the relationship between independent and dependent variables uses the Chi-Square test and the Odds Ratio (OR) with a CI95% and a significance level of p<0.050. Multivariate analysis using multilogistic regression analysis and univariate analysis to obtain the frequency distribution and percentage characteristics of the study subjects. Bivariate analysis to analyze the relationship between independent and dependent variables uses the Chi-Square test and the Odds Ratio (OR) with a CI of 95% and a significance level of p<0.050. Multivariate analysis using multiple logistic regression analysis.
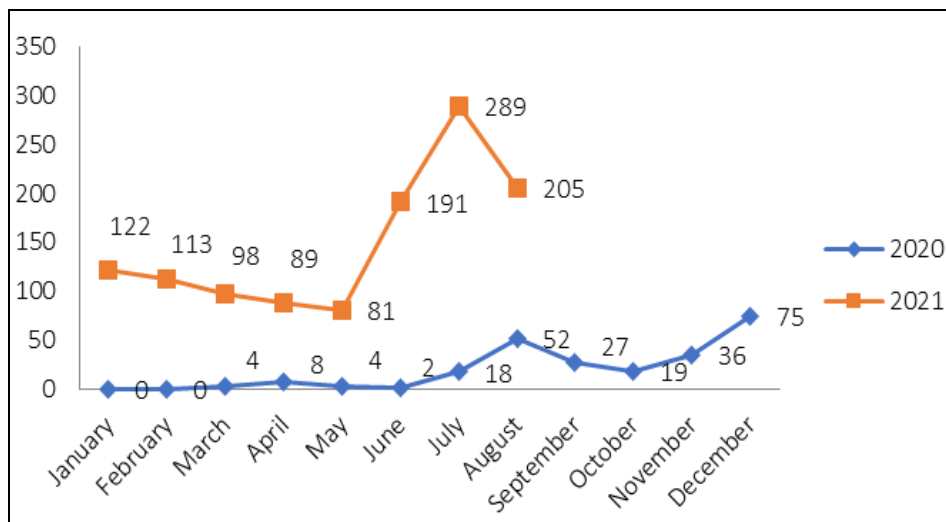

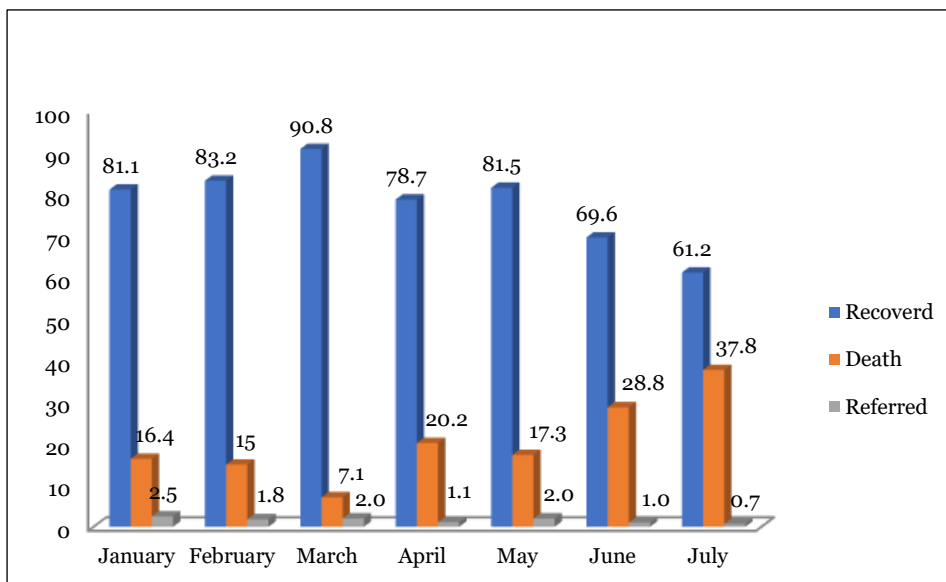**Figure 1. The Number of Hospitalized Covid-19 Cases at RSUD Panembahan Senopati Bantul**

Figure 2. The Condition of hospitalized Covid-19 cases in Panembahan Senopati General Hospital 2021

The percentage of recoveries from COVID-19 inpatients at Panembahan Senopati Bantul Hospital from January to July fluctuated. Starting in January, the

percentage of patient recoveries has increased, but from May to July, the percentage of recoveries of Covid-19 patients has decreased. In contrast to the percentage of recovery of COVID-19 patients, the percentage of deaths of COVID-19 patients from January to March has decreased. However, the percentage of deaths of Covid-19 patients has increased from May to July. In Figure 2 the highest percentage of deaths also occurred in July 2021 (37.8%).

1. Sample Characteristics

COVID-19 inpatients in July 2021 at Panembahan Senopati Hospital were 289 people with 106 deaths (36.7%). The number of male and female patients was almost equal,

with men numbering 133 (46.0%) and women numbering 156 (54.0%).The number of patients aged <60 years is more dominant than patients aged ≥60 years, which is 202 people (69.9%). Patients who had comorbid DM as many as 76 people (26.3%), hypertension in as many as 56 people (19.4%), chronic kidney failure in as many as 19 people (6.6%), heart as many as 12 people (4.2%), immunological disorders as many as 5 people (1.7%), COPD as many as 2 people (0.7%), and at least comorbid chronic liver failure as many as 1 person (0.3%). The characteristics of COVID-19 inpatients are shown in the following table.

Table 1. Sample Characteristics of Inpatient Covid-19 Patients at Panembahan Senopati Bantul Hospital

Variable	Category	Frequency	Percentage (%)
Patient Status	Death	106	36.7
	Alive	183	63.3
Gender	Male	133	46
	Female	156	54
Age	≥60 year	87	30.1
	< 60 year	202	69.9
Komorbid	Diabetes Mellitus	76	26.3
	Hypertension	56	19.4
	Chronic Renal Failure	19	6.6
	Heart	12	4.2
	Immunological disorders	5	1.7
	COPD	2	0.7
	Chronic liver failure	1	0.3
	No comorbidities	118	40.8

2. Bivariate Analysis

Table 2 shows the results of bivariate analysis that age ≥60 years (OR= 2.16; 95% CI= 1.29 to 3.60; p= 0.003), sex (OR= 1.01; 95% CI=0.63 to 0.74; p=0.957), diabetes mellitus (OR= 2.88; 95% CI= 1.68 to 4.93; p <0.001), hypertension (OR = 3.46; 95% CI = 1.89 to 6.32; p<0.001), chronic renal failure (OR= 4.12; 95%CI=1.52 to 11.20; p= 0.003), heart disease (OR= 1.77; 95% CI= 0.56 to 5.63; p= 0.328), immunological disorders (OR= 0.43;

95%CI= 0.05 to 3.86; p= 0.435), COPD (OR= 1.77; 95% CI=0.11 to 28.00; p= 0.695).

3. Multivariate Analysis

Table 3 shows the results of multivariate analysis. Table 3 shows that the variables that statistically significantly affect the mortality of hospitalized Covid-19 patients are age, diabetes mellitus, hypertension, and chronic renal failure.

Age ≥60 years was 2.13 times more likely to cause death (OR= 2.13; 95% CI =

1.24 to 3.66; p=0.006).Hospitalized COVID-19 patients with comorbid Diabetes Mellitus were 2.32 times more likely to cause death (OR= 2.31; 95% CI= 1.30 to 4.13; p= 0.004). Hospitalized Covid-19 patients with comorbid hypertension were 2.19 times more likely to cause death (OR= 2.19; 95% CI = 1.13 to 4.26; p= 0.021). Hospitalized COVID-19 patients with comorbid chronic renal failure were likely to cause 3.25 times the death (OR= 3.25; 95% CI=1.11 to 9.51; p= 0.031)).

Table 2. Bivariate Analysis of Risk Factors for Death in Hospitalized Covid-19 Patients at Panembahan Senopati Hospital, Bantul

Variable	Category	Patient Status				OR	95%CI		p
		Death		Alive			Lower Limit	Upper Limit	
		n	%	n	%				
Age	≥60 years	43	49.4	44	50.6	2.16	1.29	3.61	0.003
	<60 years	63	31.2	139	68.8				
Gender	Male	49	36.8	84	63.2	1.01	0.63	0.74	0.957
	Female	57	36.5	99	63.5				
Diabetes Mellitus	Yes	42	55.3	34	44.7	2.88	1.68	4.93	<0.001
	No	64	30.0	149	70.0				
Hypertension	Yes	34	60.7	22	39.3	3.46	1.89	6.32	<0.001
	No	72	30.9	161	69.1				
Chronic renal failure	Yes	13	68.4	6	31.6	4.12	1.52	11.20	0.003
	No	93	34.4	177	65.6				
Heart Disease	Yes	6	50.0	6	50.0	1.77	0.56	5.63	0.328
	No	100	36.1	177	63.9				
Immunological disorders	Yes	1	20.0	4	80.0	0.43	0.05	3.86	0.435
	No	105	37.0	179	63.0				
PPOK	Yes	1	50.0	1	50.0	1.73	0.11	28.00	0.695

Tabel 3. Multivariate Analysis of Risk Factors for Death in Inpatient Covid-19 Patients at Panembahan Senopati Bantul Hospital

Variabel	OR	CI 95%		p
		Lower Limit	Upper Limit	
Age (≥ 65 years)	2.13	1.24	3.66	0.006
Diabetes Mellitus	2.32	1.30	4.13	0.004
Hypertension	2.19	1.13	4.26	0.021
Chronic renal failure	3.25	1.12	9.51	0.031

DISCUSSION

1. Age ≥60 years

The age of patients who are more than 60 years old has a statistically significant effect on the mortality of hospitalized COVID-19 patients compared to the age of patients less than 60 years. This finding is similar to a study conducted by Satria et al. (2020) which stated the risk of mortality in patients over 64 years was 2.09 times higher than in patients aged less than 64 years (p= 0.041). Another study conducted by Rozaliyani et al. (2020) states that old age is associated with the risk of death (OR= 1.03; 95% CI= 1.02 to 1.05). Elderly patients and those with chronic diseases tend to experience severe COVID-19 cases and even death (Gesesew et al., 2021). The elderly are one of the at-risk populations that have health problems and will develop worse because there are influencing risk factors. Elderly patients with comorbidities need more medical needs (Saputra et al., 2021). The reserve of homeostasis function will decrease with age which

positions the elderly in conditions that are not supportive to fight aggressive infections, such as COVID-19 (Drew and Adisasmita, 2021).

2. Diabetes mellitus

In this study, the percentage of Covid-19 patients who had comorbid DM was 26.3%. Comorbid DM has a statistically significant effect on the mortality of hospitalized COVID-19 patients. This is in line with the results of research which states that comorbid DM is one of the most common factors causing the death of COVID-19 patients (Chidambaram et al., 2020). Comorbid DM is also one of the risk factors for death in Covid-19 patients (OR=4.34; p<0.001) (Satria et al., 2020) and increases the risk of death by 2.12 times higher (CI 95%= 1.44 to 3.11; p<0.001) (Ministry of Health, 2021a). Patients with a history of DM have a inhibited immune system due to chronic hyperglycemia and immune modulation disorders (Drew and Adisasmita, 2021).

Type II DM is known as a predictor of death due to COVID-19 (Kurniawati et al., 2021). ACE2 may be the main cause of COVID-19 severity in DM patients. ACE2 is a type 1 integral membrane glycoprotein expressed in epithelial cells of cardiovascular, pulmonary, kidney, brain, and intestinal tissues, working by breaking down angiotensin II into angiotensin 1e7. This enzyme works by countering the inflammatory action of angiotensin II, lowering the concentration of pro-inflammatory cytokine interleukin (IL)-6, enhancing anti-inflammatory, and enhancing the antioxidant action of angiotensin 1-7, increasing surfactant protein D levels and promoting vasodilation. The SARS-CoV-2 virus uses ACE2 to bind to and enter the host pneumocyte. The viral surface protein (S) binds to ACE2 after protein activation by transmembrane protease serine 2 (TMPRSS 2) (Huang et al., 2020).

3. Chronic renal failure

Comorbid history of chronic renal failure has a statistically significant effect on the death of hospitalized COVID-19 patients This is in line with research by Drew and Adisasmita (2021) which states that patients with chronic kidney failure, the risk of death increases up to 3.33 times higher. Chronic renal failure was associated with improved poor conditions in COVID-19 patients and increased patient mortality by 3.47 times higher (OR= 3.47; CI95%= 1.36 to 8.86) (Pranata et al., 2020b). The process of COVID-19 disease generally involves the release of inflammatory cytokines and the formation of antibody-antigen complexes that will affect cell membrane permeability. However, in patients with chronic renal failure, the glomerular filtration process has worsened, so that systemic inflammation due to Covid-19 can worsen kidney function. In addition, due to the presence of ACE2 receptors in the urogenital system, the Covid-19 virus can also easily stimulate inflammatory processes in the kidneys which will worsen the patient's condition (Drew and Adisasmita, 2021).

4. Hypertension

Comorbid hypertension is statistically significant in affecting the mortality of hospitalized Covid-19 patients. This is supported by research by Rozaliyani et al. (2020) and Chidambaran et al. (2020) which states that comorbid hypertension is associated with increased mortality in Covid-19 patients and is risk factor for death (RR= 2.21; CI95%= 1.74 to 2.81; p<0.001) (Pranata et al., 2020[a]). COVID-19 patients with a history of hypertension will further aggravate their infection (Larsiani et al., 2022). Populations with hypertension tend to have a higher number of ACE2 receptors, causing the Coronavirus to disseminate more easily in the body (Drew and Adisasmita, 2021),

thereby increasing the risk of death in COVID-19 patients (Permata et al., 2021)

The risk factors found to affect mortality in COVID-19 patients in this study were age ≥65 years, comorbid history of DM, hypertension, and chronic renal failure together can increase the probability of death in inpatient COVID-19 patients at Panembahan Senopati Hospital Bantul. The limitation of this study is that the study design uses cross-sectional, namely data obtained at one time so that there are no observations in the long term and other factors such as D-Dimer values, socio-demographics and clinical conditions are not observed in this study.

AUTHOR CONTRIBUTION

Christiana contributed as the principal investigator, data collector, data processing, data analysis, and script writing, Ledy contributed to help collect data and write the script, Esthi contributed to planning and supervising the research process and Ria contributed to help collect data.

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CONFLICT OF INTEREST

There was no conflict of interest in this study.

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