THE RELATIONSHIP BETWEEN DIABETES MELLITUS AND MORTALITY RISK IN COVID-19 PATIENTS IN PALEMBANG CITY

Yulia Yunara[1] , Yeni[2], Najmah[3], Amrina Rosyada[4], Yudhi Setiawan[5], Fauzia[6], Yuliarni[7]

[1,2,3,4]Faculty of Public Health, Universitas Sriwijaya, Jl. Palembang Prabumulih KM 32, Indralaya, South Sumatera 30662, Indonesia
[5,6,7]Palembang City Health Office, Jl. Merdeka No.72, 22 Ilir, Kec. Bukit Kecil, Palembang, South Sumatera, Indonesia
* Correspondence Author: yenidoanks88@gmail.com

ABSTRACT

COVID-19 is a new disease which is declared as a pandemic in March, 2020. The deaths caused by COVID-19 are assumed to be accompanied by several other risk factors. This reserch purpose aims to analyze the relationship between diabetes. This is quantitative research used secondary data from the Palembang City Epidemiological Surveillance System (SISUGI), with a cross-sectional research design. The sample was COVID-19 patient in Palembang City with complate data, from March 2020-march 2021 with 1227 people. The results of an examination on 1227 COVID-19 patients in Palembang show that 4.6% of them have diabetes mellitus and 5.6% of them passed away. Results of the bivariate test, it is found that there is a relationship between diabetes mellitus (P-value < 0.001), age over 60 years (P-value < 0.001), hypertension (P-value < 0.001), heart disease (P-value < 0.001), kidney failure (P-value < 0.001) and COPD (P-value = 0.06; CI = 1.4-16.7) with risk of death in COVID-19 patients in Palembang. Multivariate analysis show that there is a significant relationship between diabetes mellitus and risk of death in COVID-19 patients in Palembang (P-value < 0.001) after controlling the age, heart disease, hypertension, kidney failure and malignancy elements (RR= 6.113; 95% CI= 2.978- 12.54). There is a significant between diabetes mellitus with risk of death in COVID-19 patients in Palembang. This results of this research can serve as the foundation to prevent COVID-19 in at-risk groups - such as people with diabetes mellitus.

Key word **:** Diabetes Mellitus, COVID-19, Risk of Death, COVID-19 patients

Introduction

COVID-19 or corona virus has now become a disease whose spread occurs globally or worldwide with an increasing number of cases. Since the first announcement was identified in December 2019 in the city of Wuhan, Hubei Province of China, then the World Health Organization (WHO) officially declared COVID-19 a pandemic in March 2020, precisely on the 11th [1]. One of the impacts in the health sector is the continued increase in the death rate due to COVID-19. In Indonesia, deaths due to COVID-19 also continue to increase, as of July 2021 there were more than 66 thousand deaths, with a crude death rate or case fatality rate of 2.6%. Indonesia is in the 3rd position with the highest number of deaths from COVID-19 in Asia [2] (Worldmeters, 2021).

Deaths due to COVID-19 were followed by several other factors, most of the COVID-19

patients who died had congenital diseases and were also elderly patients. From patient data, positive confirmation in Indonesia is hypertension, but in cases of patients who die, the comorbidity most often experienced by patients is diabetes mellitus[3]. Diabetes mellitus is a non-communicable disease whose number of sufferers continues to increase every year, both in Indonesia and in the world. Based on data from the International Diabetes Federation (IDF) in the 2019 IDF Atlas, as many as 463 million people worldwide live with diabetes mellitus. Indonesia is ranked 7th in the country with the highest diabetes mellitus rate in adults, it is estimated that there are 10.7 million people in Indonesia with diabetes mellitus [4]. Several studies have stated that there is a relationship between diabetes mellitus and the severity and also death in COVID-19 patients. The study, which was conducted using the meta-analysis method, showed that diabetes mellitus was significantly associated with the death of COVID-19 patients with an OR of 1.90 (95% CI: 1.37-2.64; p <0.01). Diabetes mellitus was also associated with severity in COVID-19 patients with OR 2.75 (95% CI: 2.09-3.62; p <0.01) [5]. Then there is also a study conducted at a hospital in Italy, the results of which showed that diabetes mellitus was significantly associated with death in COVID-19 patients with an RR value (RR 1.56; 95% CI 1.05-2.02)[6].

Based on this description, this study wanted to see the relationship between diabetes mellitus and the risk of death in COVID-19 patients in Palembang City. Palembang City is currently the highest region for positive confirmed cases and COVID-19 death cases in South Sumatra Province. The death rate due to COVID-19 in the city of Palembang has currently reached 800 cases and is still growing.

Methods

This research is a quantitative research with a cross sectional study design. The data used in this research is a type of secondary data, namely data from epidemiological investigations of COVID-19 patients in Palembang City. The samples from this study were patients confirmed positive for COVID-19 who were recorded in the Epidemiological Surveillance System of the Palembang City Health Service and met the inclusion criteria. The inclusion criteria for this study were that the patient tested positive for COVID-19, had complete epidemiological records, and the patient's status was declared cured or dead. This study took data from the SISUGI system with data ranging from March 2020 to March 2021. From 8309 initial data on COVID-19 patients contained in the system

SISUGI, after processing, the final data was obtained for 1227 patients. Data analysis in this study includes univariate, bivariate and multivariate analysis.

Results

Table 1. Characteristics of COVID-19 Patients in Palembang City

Category	Frequency	Percentage (%)
Covid patient status		
Death	64	5,2
Recovered	1163	94,8
Age		
>60 years	166	13,5
≤60 years	1061	86,5
Sex		
Man	645	52,6
Woman	582	47,4
Comorbid		
Diabetes mellitus	57	4,6
Heart disease	32	2,6
Hypertension	95	7,7
Cancer	2	0,2
Gagal Ginjal	6	0,5
PPOK	8	0,7

Source: Epidemiological Surveillance Information System (Sisugi), March 2020-March 2021

There are more Covid-19 patients in Palembang City (52.6%) than women (47.4%), with 166 people aged over 60 years (13.5%), and 64 patients COVID-19 (5.2%) experienced deaths. Judging from the comorbidities suffered by patients, 57 people (4.6%) had comorbid diabetes mellitus, 95 patients had comorbid hypertension (7.7%), 32 patients had comorbid heart disease (2.6%). %), only 2 patients (0.2%) had comorbid malignancy/cancer, 6 patients with comorbid kidney failure were known (0.5%), Finally, there were 8 patients with comorbid COPD (0.7%).

Table 2. Bivariate Analysis of Risk Factors for Death of COVID-19 Patients in Palembang City

Variable		Covid patient status				Total (%)	P-Value (95%CI)
		Death		Recovered			
		n	%	n	%		
Sex	Man	40	6,2	605	93,8	100.0%	0,1 (0,9-2,5)
	Woman	24	4,1	558	95,9	100.0%	
Age	> 60	29	17,5	137	82,5	100.0%	<0,001
	≤ 60	35	3,3	1026	96,7	100.0%	(3,3-8,4)
Diabetes	Yes	17	29,8	40	50,4	100.0%	<0,001
	No	47	4	1123	96	100.0%	(4,6-12,1)
Hypertension	Yes	23	24,2	72	75,8	100.0%	<0,001 (4,2-10,6)
	No	41	5,2	1163	94,8	100.0%	
Heart disease	Yes	12	37,5	20	62,5	100.0%	<0,001
	No	52	4,4	1143	95,6	100.0%	(5,1-14,5)
Cancer	Yes	1	50	1	50	100.0%	0,1
	No	63	5,1	1162	94,9	100.0%	(2,4-39,7)
Kidney failure	Yes	4	66,7	2	33,3	100.0%	<0,001
	No	60	4,9	1161	95,1	100.0%	(7,3-25,1)
Chronic Obstructive Pulmonary Disease (COPD) (PPOK)	Yes	2	25	6	75	100.0%	0,06
	No	62	5,1	1157	94,9	100.0%	(1,4-16,7)

Source: Epidemiological Surveillance Information System (Sisugi), March 2020-March 2021

From the results of the bivariate test, was there a significant relationship between diabetes mellitus (P-value <0.001), age over 60 years (P-value <0.001), hypertension (P-value <0.001), heart disease (P-value < 0.001), kidney failure (P-value <0.001) and COPD (P-value = 0.06; CI = 1.4-16.7) with the risk of death for COVID-19 patients in the city of Palembang.

Table 3. Multivariate Analysis of the Relationship between Diabetes Mellitus and Death of COVID-19 Patients in Palembang City

Variable	*P-Value*	RR	95% CI
Diabetes	<0,001	6,113	2,978-12,54
Age	<0,001	3,656	2,015-6,634
Heart disease	0,012	3,407	1,315-8,824
Hypertension	0,002	3,021	1,479-6,168
Kidney failure	0,001	25,54	3,570-182,7
Cancer	0,036	23,37	1,233-443,0

Source: Epidemiological Surveillance Information System (Sisugi), March 2020-March 2021

Based on table 4.20, the results of the multivariate analysis found that there was a significant relationship between diabetes mellitus and the risk of death for COVID-19 patients in Palembang City after controlling for the variables age, heart disease, hypertension, kidney failure and malignancy/cancer. In this study, COVID-19 patients with diabetes mellitus increased their risk of death by 6,113 times. For the general public, the risk ranges from 3.086 to 13.114 times greater in dying from COVID-19 if you have comorbid diabetes

Discussion

From research that has been conducted, there is a significant relationship between diabetes mellitus and the risk of death in COVID-19 patients. Many previous studies have also stated that there is a relationship between diabetes mellitus and death in Covid-19 patients. In a study conducted in China, COVID-19 patients with diabetes mellitus were more likely to have severe or critical conditions, complications and death, the risk of death was up to 3 times higher in patients with diabetes mellitus [7]. In addition to research conducted at the Massachusetts General Hospital (MGH), patients with diabetes mellitus have up to 1.6 times more chances to enter the ICU, and 2 times more likely to die [8]. Then there was research conducted using data from 828 Covid-19 patients in various regions of the world which stated that diabetes mellitus increased the risk of death up to 12 times higher. [9].

Diabetes mellitus in Covid-19 patients is associated with a weakening of the immune system, causing various inflammations or infections. Metabolic disorders that occur in diabetes mellitus sufferers can disrupt macrophages and lymphocytes, which means the body's immunity will weaken[10]. In Covid-19 patients with Diabetes mellitus there are more infections, especially influenza and pneumonia [11].

Diabetes mellitus may also have an impact on Covid-19 patients because it has an influence

on the entry route for the Sars-Cov 2 Virus. The protein receptor used by the Sars-Cov 2 Virus is angiotensin-converting enzyme 2 (ACE2), which is an enzyme involved in several functions. physiology including glucose metabolism which is modulated by hyperglycemia and also drugs commonly consumed by people with diabetes mellitus. Treatment with RAS blockers is known to increase the expression of angiotensin-converting enzyme 2 (ACE2)[12]. Apart from that, diabetes can increase the production of plasmin, which can cut the S protein in the Sars Cov 2 Virus so that it binds more easily to ACE2. Plasmin also breaks down fibrin, causing increased levels of D-dimer and other degradation products that characterize the severity of the infection. [13].

The negative impact of diabetes in COVID-19 patients may not only occur due to hyperglycemia but can also occur due to other comorbidities that are also related to diabetes itself. Comorbidities usually associated with diabetes are hypertension, including chronic kidney failure and cardiovascular disease [14]. As is known, diabetes mellitus is a parent disease that provokes other diseases to attack when a patient has diabetes mellitus. The longer a person suffers from diabetes mellitus, the more complications will occur in sufferers [15] .

One of the complications of diabetes that is often suffered is hypertension. In a journal, it was stated that the percentage of diabetes patients who simultaneously also suffer from hypertension reaches 40% -60%.[16.] Hypertension itself is one of the common comorbidities found in COVID-19 patients in Indonesia, data in Indonesia shows that COVID-19 patients with hypertension reach 49.9%[3]. In this study, 57 COVID-19 patients had diabetes mellitus, 20 of whom also had hypertension, 8 of whom died. Research conducted in Wuhan, China, showed a 2-fold increase in the risk of death in Covid-19 patients with hypertension [17.]

Apart from hypertension, another complication that can occur in people with diabetes mellitus is heart disease. Diabetics are known to be two to four times more at risk for developing coronary heart disease[18]. In this study there were 7 diabetes mellitus patients who also had heart disease, 3 of these patients died. Coronary heart disease itself is also related to COVID-19, a study states that COVID-19 patients with coronary heart disease have a 3 times higher risk of death[19].

Diabetes mellitus is also associated with renal failure, chronic renal failure in diabetics occurs due to diabetic nephropathy or can be due to other related conditions such as hypertension, dysfunctional bladder polyneuropathy, increased incidence of recurrent urinary tract infections, or macrovascular angiopathy. In the United States it is estimated that there are 25% of people with diabetes mellitus, 36% of whom have chronic renal failure, with 9% having a severe event[20]. In this study, there were 3 COVID-19 patients with diabetes mellitus who also had kidney failure, 2 of these patients died. Kidney failure is one of the comorbidities that can be found in COVID-19 patients, kidney failure is also one of the diseases that can exacerbate COVID-19 patients, in a study conducted by Ozturk et al. (2020) states that COVID-19 patients with kidney failure have a risk of death 3 times higher than patients who do not have kidney failure (95% CI 1.524-5.442)[21].

Apart from that, the severity and risk of death of COVID-19 patients with diabetes mellitus can also be influenced by the age factor of those who have entered old age. In this study, it was discovered that there were 23 COVID-19 patients with diabetes mellitus who had also entered old age, with 7 of them dying. The worsening health of COVID-19 patients with diabetes mellitus and old age can also be seen in the results of research conducted in South Korea which shows that the severity of the disease will increase up to 17 times higher in patients over 70 years of age [22]. In addition, based on research conducted by Mohitosh Biswas in 2020, COVID-19 patients who are more than 50 years old have a 15.4 times higher risk of death compared to patients aged less than 50 years (RR 15.44; 95% CI 13 .02-18.31;p < 0.00001)[23].

The finding that there is a relationship between diabetes mellitus and the risk of death in COVID-19 patients indicates the need for prevention and control measures. Management of diabetes mellitus in sufferers must be done to prevent diabetes mellitus from getting worse which can then result in various other complications. In addition, COVID-19 patients with diabetes mellitus who have good management can prevent the risk of death from COVID-19. This was mentioned in Zhu L's study which stated that patients with good diabetes mellitus control had a lower risk of death compared to COVID-19 patients with poor diabetes mellitus control[24]. Benerjee and Chakraborty, (2020) in their article on self-management of diabetes mellitus sufferers during a pandemic wrote that diabetics must have a good dietary pattern, the recommended diet is one that is adapted to daily calorie needs and avoids foods with preservatives and artificial sweeteners. Apart from that, it is also recommended to carry out daily physical activity with an intensity and type that is adjusted to your fitness

individual abilities. Next, undergo appropriate treatment, finally continue to monitor the blood sugar levels of diabetes mellitus sufferers [25].

Conclusion

In this study, COVID-19 patients in Palembang City had diabetes mellitus as many as 4.6% with patients aged more than 60 years or called elderly by 13.3%, male patients as much as 52.6%; the remaining 47.4% were female patients, 7.7% of patients with hypertension, 2.6% of heart disease, 0.5% of kidney failure, 0.2% of malignancy/cancer, and finally 0.7% of patients with COPD, Palembang City COVID-19 patients who died were 5.2%. In COVID-19 patients who also have diabetes mellitus, the death rate is 28.9%. Of the existing variables, the variables that are significant with the risk of death for COVID-19 patients in Palembang City are Diabetes mellitus (P-value <0.001; RR=7.4; 95% CI = 4.6-12.1), older age than 60 years (P-value <0.001; RR=5.3; 95% CI = 3.3-8.41), hypertension (P-value <0.001; RR=6.7; 95% CI = 4.2 -10.6), heart disease (P-value <0.001; RR=8.6; 95% CI = 5.1-14.5), kidney failure (P-value <0.001; RR=13.6; 95 % CI = 7.3-25.1) and COPD (P-value = 0.06; RR = 4.9; 95% CI = 1.4-16.7). For the diabetes mellitus

variable, based on the results of multivariate analysis, it showed a significant relationship to the risk of death for COVID-19 patients in Palembang City (P-value <0.001) after controlling for age, heart disease, hypertension, kidney failure and malignancy.

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Conflict of Interest

There is no conflict of interest in this research.

Reference

1. WHO. Critical preparedness, readiness and response actions for COVID-19 [Internet]. 2020. Available from: https://apps.who.int/iris/handle/10665/331511?search-result=true&query=Critical+preparedness%2C+readiness+and+response+actions+for+COVID-19&scope=&rpp=10&sort_by=score&order=desc
2. Wordometers. COVID-19 CORONAVIRUS PANDEMIC, [Internet]. 2021. Available from: https://www.worldometers.info/coronavirus/
3. Covid19.go.id. Peta Sebaran COVID-19 [Internet]. 2021. Available from: https://covid19.go.id/peta-sebaran-covid19
4. IDF. IDF DIABETES ATLAS Ninth edition 2019. International Diabetes Federation; 2019.
5. Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, et al. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. Diabetes Metab Syndr Clin Res Rev. 2020;14(4):535–45.
6. Ciardullo S, Zerbini F, Perra S, Muraca E, Cannistraci R, Lauriola M, et al. Impact of diabetes on COVID-19-related in-hospital mortality: a retrospective study from Northern Italy. J Endocrinol Invest. 2021;44(4):843–50.

7. Zhang Y, Cui Y, Shen M, Zhang J, Liu B, Dai M, et al. Association of diabetes mellitus with disease severity and prognosis in COVID-19: A retrospective cohort study. Diabetes Res Clin Pract. 2020 Jul;165:108227.
8. Seiglie J, Platt J, Cromer SJ, Bunda B, Foulkes AS, Bassett I V, et al. Diabetes as a Risk Factor for Poor Early Outcomes in Patients Hospitalized With COVID-19. Diabetes Care. 2020;43(12):2938–44. Available from: https://doi.org/10.2337/dc20-1506
9. Albitar O, Ballouze R, Ooi JP, and Ghadzi SM. Risk Factors For Mortality Among COVID-19 Patients. Diabetes Research and Clinical Practice. 2020;166: Article 108293.
10. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. International Journal of Infectious Diseases, 2020;94:91–95.
11. Gupta R, Ghosh A, Singh A.K. and Misra A. Clinical considerations for patients with diabetes in times of COVID-19 epidemic. Diabetes & metabolic syndrome. 2020;14(3):211–212.
12. Bavishi C, Maddox TM, Messerli FH. Coronavirus Disease 2019 (COVID-19) Infection and Renin Angiotensin System Blockers. JAMA Cardiol. 2020 Jul 1;5(7):745–7. Available from: https://doi.org/10.1001/jamacardio.2020.1282
13. Ji H-L, Zhao R, Matalon S, Matthay MA. Elevated Plasmin(ogen) as a Common Risk Factor for COVID-19 Susceptibility. Physiol Rev. 2020 Jul;100(3):1065–75.
14. Pugliese G, Vitale M, Resi V, Orsi E. Is diabetes mellitus a risk factor for COronaVIrus Disease 19 (COVID-19). Acta Diabetol. 2020;57(11):1275–85. Available from: https://doi.org/10.1007/s00592-020-01586-6
15. Lathifah NL. Hubungan Durasi Penyakit Dan Kadar Gula Darah Dengan Keluhan Subyektif Penderita Diabetes Melitus. Berkala Epidemiologi. 2017 Agust;5(231-239).
16. Ayutthaya S, and Adnan N. Faktor Risiko Hipertensi pada Penderita Diabetes Mellitus Tipe 2. Jurnal Ilmu Kesehatan Masyarakat. 2020; 9(02):60–71.
17. Mubarik S, Liu X, Eshak ES, Liu K, Liu Q, Wang F, et al. The Association of Hypertension With the Severity of and Mortality From the COVID-19 in the Early Stage of the Epidemic in Wuhan, China: A Multicenter Retrospective Cohort Study. Frontier in Medicine. 2021;8: Article 623608.
18. Yulani F, Oenzil F, and Iryani D. Hubungan Berbagai Faktor Risiko Terhadap Kejadian

Penyakit Jantung Koroner Pada Penderita Diabetes Melitus Tipe 2. Jurnal Kesehatan Andalas. 2014;3(1):37-40.

19. Loffi M, Piccolo R, Regazzoni V, Di Tano G, Moschini L, Robba D, et al. Coronary artery disease in patients hospitalised with Coronavirus disease 2019 (COVID-19) infection. Open heart, 2020;7(2).
20. IDF. IDF DIABETES ATLAS 10th Edition. International Diabetes Federation; 2021.
21. Ozturk S, Turgutalp K, Arici M, Odabas AR, Altiparmak MR, Aydin Z, et al. Mortality Analysis Of COVID-19 Infection In Chronic Kidney Disease, Haemodialysis and Renal Transplant Patients Compared with Patients Without Kidney Disease: A Nationwide Analysis From Turkey. Nephrol Dial Transplant. 2020 Dec 4;35(12):2083-2095.
22. Acharya D, Lee K, Lee DS, Lee YS, Moon SS. Mortality Rate and Predictors of Mortality in Hospitalized COVID-19 Patients with Diabetes. Healthcare (Basel). 2020 Sep 13;8(3):338.
23. Biswas M, Rahaman S, Biswas T.K, Haque Z. and Ibrahim B. Association of Sex, Age, and Comorbidities with Mortality in COVID-19 Patients: A Systematic Review and Meta-Analysis. Intervirology. 2021;64(1):36–47.
24. Zhu L, She Z.-G, Cheng X, Qin J-J, Zhang X-J, Cai J et al. Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metabolism, 2020; 31(6):1068–1077.
25. Banerjee M, Chakraborty S, Pal R. Diabetes self-management amid COVID-19 pandemic. Diabetes Metab Syndr. 2020 Jul-Aug;14(4):351-354.