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THE RELATIONSHIP OF DIABETES MELLITUS AND HYPERTENSION WITH MORTALITY IN COVID-19 PATIENTS

Hubungan Diabetes Melitus dan Hipertensi dengan Kematian pada Pasien COVID-19

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) can infect the human respiratory system and causes 6.93% of all deaths in East Java Province. Comorbid diabetes mellitus and hypertension can exacerbate COVID-19 patients. **Purpose:** This study aims to analyze the relationship between diabetes mellitus and hypertension with mortality in COVID-19 Patients in Lamongan District. **Methods:** This study used an analytic observational study with a cross-sectional design. The study population was patients diagnosed with COVID-19 and registered at Lamongan District Health Office from April to August 2020, as many as 412 patients. The study sample was 93 patients who were taken by simple random sampling. The dependent variable in the study was the incident of mortality in COVID-19 patients. The independent variables in the study were gender, age, hypertension, and diabetes mellitus. Data analysis was using the chi-square test. **Results:** The variables studied that had a relationship with mortality in COVID-19 patients were age ≥ 60 years (p = 0.02; PR = 3.23; 95% CI = 1.29 <PR <8.10) and diabetes mellitus (p = 0.03; PR = 3.20; 95% CI = 1.23 <PR <8.36). The variables studied that did not have a relationship with mortality in COVID-19 patients were gender (p = 0.30; PR = 1.72; 95% CI = 0.74 <PR <4.03) and hypertension (p = 0.72; PR = 1.37; 95% CI = 0.34 <PR <5.48). **Conclusion:** Age and diabetes mellitus are significantly associated with mortality in COVID-19 patients, but sex and hypertension are not significantly associated with mortality in COVID-19 patients.

ABSTRAK

*Latar Belakang: Corona virus disease 2019 (COVID-19) dapat menginfeksi sistem pernafasan manusia dan menyebabkan 6,93% kematian di Provinsi Jawa Timur. **Tujuan:** Penelitian ini bertujuan untuk menganalisis hubungan diabetes melitus dan hipertensi dengan kejadian kematian akibat penyakit COVID-19 di Kabupaten Lamongan. **Metode:** Penelitian menggunakan jenis penelitian observasional analitik dengan desain cross-sectional. Populasi dalam penelitian adalah semua pasien yang terdiagnosis COVID-19 dan tercatat di Dinas Kesehatan Kabupaten Lamongan pada bulan April – Agustus 2020 sebanyak 412 pasien. Teknik pengambilan sampel dengan simple random sampling dan didapatkan sebanyak 93 pasien menjadi sampel penelitian. Variabel terikat dalam penelitian adalah status kematian pada pasien COVID-19. Variabel bebas dalam penelitian adalah jenis kelamin, usia, hipertensi, dan diabetes melitus. Data dianalisis dengan uji chi-square. **Hasil:** Variabel diteliti yang memiliki hubungan dengan kematian pada pasien COVID-19 adalah usia ≥ 60 tahun (p = 0,02; PR = 3,23; 95% CI = 1,29 < PR < 8,10) dan diabetes melitus (p= 0,03; PR = 3,20; 95% CI = 1,23 < PR < 8,36). Variabel diteliti yang tidak memiliki hubungan dengan kematian pada pasien COVID-19 adalah jenis kelamin (p= 0,30; PR =1,72; 95% CI = 0,74 < PR < 4,03) dan hipertensi (p= 0,72; PR = 1,37; 95% CI = 0,34 < PR < 5,48). **Kesimpulan:** Usia dan diabetes melitus berhubungan signifikan dengan kematian pada pasien COVID-19, namun jenis kelamin dan hipertensi tidak berhubungan secara signifikan terhadap kematian pada pasien COVID-19.*

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a new disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), where the mode of transmission is relatively easy and fast through droplets (splashes of saliva) or direct contact with infected surfaces (Gorbalenya et al., 2020; Tian et al., 2020). This disease attacks the human respiratory system and causes severe respiratory problems that have the potential to cause death in the sufferer. The symptoms experienced by COVID-19 patients are quite diverse; 97.86% of COVID-19 patients have a fever, 76.21% of patients have a cough, and 54.69% of patients have dyspnea (Grace, 2020).

COVID-19 is categorized as a global pandemic because of a considerable increase in cases worldwide. COVID-19 cases in Indonesia are relatively high; on 3rd February 2021 as many as 1,111,671 people were confirmed positive for COVID-19, and 30,770 people (2.77%) died (Ministry of Health RI, 2021). East Java is one of the provinces affected by COVID-19. On 30th January 2021, 111,939 people were confirmed positive for COVID-19, and 7,754 people (6.93%) died. Lamongan is one of the regencies in East Java Province affected by COVID-19 (COVID-19 Handling Task Force Unit of East Java, 2021).

Diabetes mellitus and hypertension are risk factors for death in COVID-19 patients. Based on data from the COVID-19 Handling Task Force Unit (2021) patients who died from COVID-19 in East Java Province, 5.32% of patients suffered from diabetes mellitus and 4,68% suffered from hypertension. Diabetes mellitus and hypertension are diseases that are suffered by many people and one of the most common comorbidities found in COVID-19 patients. Individuals suffering from diabetes mellitus in Lamongan Regency are 83.33% (Rosidah & Mahmudah, 2017), and 61.36% suffer from hypertension (Laily, 2017).

Diabetes mellitus is one of the top 3 degenerative diseases that cause several deaths in Indonesia (Ministry of Health RI, 2018). The prevalence of diabetes mellitus increases in old

age. It has been proven that 60% of the old age group in China suffer from diabetes mellitus and prediabetics (Zhao et al., 2016). People with diabetes mellitus are not only susceptible to COVID-19 infection but also at high risk of having a poor prognosis and causing death. Research conducted in the United States on 28th March 2020 showed diabetes mellitus as a common comorbid found in patients with COVID-19, as much as 10,87% (Chow et al., 2020). The risk of death in COVID-19 patients is 2,12 times higher in individuals who have diabetes mellitus comorbid than in patients who do not have diabetes mellitus comorbid (Huang, Lim, & Pranata, 2020). Patients with diabetes mellitus are more likely to suffer from serious infections due to hyperglycemia, chronic inflammation, and impaired microcirculation (Yang et al., 2020).

Hypertension is the number one cause of death globally and a risk factor for someone infected with other diseases (Ministry of Health RI, 2019). The risk of death in COVID-19 patients is 2.42 times greater in patients with hypertension comorbid compared to non-hypertensive patients (Lippi, Wong, & Henry, 2020). Hypertension triggers the emergence of other diseases that can worsen the condition of COVID-19 patients. According to a study conducted by Shah et al. (2020) in Georgia, COVID-19 patients with hypertension comorbid had died of 93.48%.

The number of deaths due to COVID-19 in the Lamongan Regency is quite high. Some prevention efforts are needed to avoid an increased risk of death in COVID-19 patients. Research on diabetes mellitus and hypertension as risk factors for death in COVID-19 patients can be used as recommendations to prevent COVID-19 in public health sectors. This study investigates the relationship between diabetes mellitus and hypertension with the incidence of COVID-19 death in the Lamongan District.

METHODS

This study includes an analytic observational with a cross-sectional design. The population were all patients diagnosed with COVID-19 and recorded at the Lamongan District Health Office in April - August 2020. There were 412 patients registered in that month's range. The sampling technique was simple random sampling and obtained as many as 93 patients as research samples. The sampling process utilized computer software using the RandBetween function, where all populations were numbered, and then the choice of random numbers was adjusted to the required number of samples. The inclusion criteria used for the selection of this study were patients diagnosed with COVID-19 in the age group ≥ 15 years, domiciled in Lamongan Regency, and complete patient data were available. The data was secondary from the list of COVID-19 case data at the Lamongan District Health Office.

The dependent variable in this study was the death status of individuals with COVID-19 diagnosed. The independent variables used were gender, age, hypertension comorbid, and diabetes mellitus comorbid. Age was categorized into two groups: people aged≥ 60 years and age < 60 years. Gender was categorized into two, male and female. Hypertension comorbid and diabetes mellitus comorbid were also categorized into two, "yes and no". Death status was categorized into two groups, dead and alive. Variables of age, gender, hypertension comorbid and diabetes mellitus comorbid were obtained from the list of COVID-19 patient records in Lamongan District.

This research passed the ethical test at the Ethics Commission of the Faculty of Dentistry, Universitas Airlangga, with ethics number 151/HRECC.FODM/IV/2021. The principle in this research was anonymity (without a name) and confidentiality (confidentiality). After all the data were collected, data processing was carried out. It was started with editing, coding, and cross-tabulation. Data analysis in this study was carried out in univariate, bivariate and multivariate. Univariate analysis was used to present research variables in frequency tables. Bivariate analysis was beneficial to see the relationship between research variables in the form of a 2x2 table utilizing the chi-square test. Meanwhile, multivariate analysis was used to determine the dominant factor in the study using a logistic regression test.

RESULTS

The results of descriptive analysis describe the majority of respondents who participated in the study were male (51.61%). The majority of respondents are ≥ 60 years old, where the youngest is 15 years old, and the oldest is 77 years old. The majority of respondents did not have diabetes mellitus comorbid (74.19%) and hypertension (90.32%) (Table 1).

Table 2 shows COVID-19 patients in the age group of ≥ 60 years who have died (45.71%). The result of the chi-square analysis was obtained a p-value of 0.02 (p <0.05). It means that there is a

significant relationship between age and death in COVID-19 patients. The Prevalence Ratio (PR) value is 3.23 (1.29-8.10), which means that COVID-19 patients in the age group of ≥ 60 years are 3.23 times more risk of dying than COVID-19 patients in the age group < 60 years.

Table 1
Characteristics of Gender, Age, Comorbidities, and Death Status of Respondents

Variable	n	%
Gender		
Male	48	51.61
Female	45	48.39
Age (years)		
15-30	13	13.98
31-45	26	27.96
45-59	26	27.96
≥ 60	28	30.10
Diabetes Mellitus		
Yes	24	25.81
No	69	74.19
Hypertension		
Yes	9	9.68
No	84	90.32
Total	93	100.00

Table 2 shows that most COVID-19 patients who died were male (60.00%). The results of the chi-square analysis obtained a p-value of 0.30, which indicates there is no significant relationship between gender and mortality in COVID-19 patients. Table 2 shows COVID-19 patients who have diabetes mellitus comorbid and who have died (40.00%). The results of the chi-square analysis obtained a p-value of 0.03. It means that there is a significant relationship between diabetes mellitus comorbid and death in COVID-19 patients. The Prevalence Ratio (PR) value of 3.20 (1.29-8.10) means that COVID-19 patients with diabetes mellitus comorbid are 3,20 times more likely to die than COVID-19 patients who do not have diabetes mellitus comorbid. Table 2 shows COVID-19 patients who had comorbid hypertension and died (11.43%). The results of the chi-square analysis obtained a p-value of 0,72, which means that there is no significant relationship between hypertension comorbid and death in COVID-19 patients.

Table 3 is the results of logistic regression show that there is a significant relationship between age (p = 0.03 < 0.05), and diabetes mellitus comorbid (p = 0.04 < 0.05) and mortality in COVID-19 patients. The Prevalence Ratio (PR) value for age 2.80 (1.08 – 7.22) means that COVID-19 patients in the age group ≥ 60 years are 2,80 times more likely to die than COVID-19 patients in the age group < 60 years. The Prevalence Ratio (PR) value for diabetes mellitus comorbid is 2.72 (1.01 – 7.35), meaning that COVID-19 patients who have diabetes mellitus comorbid are 2,72 times more likely to die than COVID-19 patients who do not have diabetes mellitus comorbid.

Table 2
Cross-Tabulation between the Dependent Variable and the Independent Variable

Variable	Dead		Alive		Total		*p value*	PR (95% CI)
	n	%	n	%	n	%		
Age (years old)								
≥ 60	16	45.71	12	20.69	28	30.11	0.02	3.23
< 60	19	54.29	46	79.31	65	69.89		(1.29<PR<8.10)
Gender								
Male	21	60.00	27	46.55	48	51.61	0.30	1.72
Female	14	40.00	31	53.45	45	48.39		(0.74<PR<4.03)
Diabetes Mellitus								
Yes	14	40.00	10	17.24	24	25.81	0.03	3.20
No	21	60.00	48	82.76	69	74.19		(1.23<PR<8.36)
Hypertension								
Yes	4	11.43	5	8.62	9	9.68	0.72	1.37
No	31	88.57	53	91.38	84	90.32		(0.34<PR<5.48)
Total	35	100.00	58	100.00	93	100,00		

Table 3
Logistic Regression Dominant Factors of Death in COVID-19 Patients

Variable	*p*	PR	95% CI
Age	0.03	2.80	1.08 – 7.22
Diabetes Mellitus	0.04	2.72	1.01 – 7.35

DISCUSSION

Relationship Between Age and Death in Patients COVID 19

This study shows that older age ($\geq$ 60 years) is significantly associated with the incidence of death in patients with COVID-19. The results of this study are similar to the research of Shim, Mizumoto, Choi, & Chowell (2020), which showed that there was a relationship between old age ($\geq$ 60 years) and the incidence of death in COVID-19 patients. A person aged 60 years will increase the risk of death 42,10 times greater than someone aged < 60 years. The increased risk of death is evident in the older age group and will continue to improve the age.

Cases of death increase in the elderly group because older people have more comorbidities that can increase the risk of being infected with COVID-19 disease and experience severity and even death which is characterized by the emergence of Acute Respiratory Distress Syndrome (ARDS), septic shock, and dyspnea. It is because the physiology of the old age group is aging, so the function of their organs does not work properly, and the immune system decreases (Yanez, Weiss, Romand, & Treggiari, 2020). Another condition that underlies the increased risk of death in the elderly with COVID-19 is endothelial dysfunction leading to organ dysfunction (Welch & Geriatric Medicine Research Collaborative, 2021).

Relationship between Sex and Death in COVID-19 Patients

The majority of respondents who experienced death were male. The analysis results showed that there was no significant relationship between gender and the incidence of death in COVID-19 patients. This study is in line with Wu et al. (2020), which stated that death in COVID-19 patients mostly occurred in the male gender by 65.91%, and there was no relationship between gender and death in COVID-19 patients. Men and women have the same significant risk of dying from being infected with COVID-19. The results of this study are different from the research of

Rozaliyani et al. (2020) conducted in DKI Jakarta Province in March - April 2020. This study showed a significant relationship between gender and death in COVID-19 patients. Mortality increases in males compared to females due to differences in hormones and enzymes that can affect individual immunity and differences in comorbidities, wherein males are more likely to suffer from life-threatening comorbidities such as cardiovascular and chronic lung disease. In contrast, women suffer from chronic non-fatal comorbidities such as migraine and musculoskeletal disorders (Salah & Mehta, 2021).

Differences in lifestyle, smoking habits, social roles, and the intensity of contact with other people between male and female sexes also affect the incidence of death in COVID-19 patients (Ahrenfeldt, Otavova, Christensen, & Lindahl-Jacobsen, 2021). The difference in the study results could be because there were fewer COVID-19 patients who died than those who survived.

Relationship of Diabetes Mellitus Comorbid with Death in COVID-19 Patients

This study showed that diabetes mellitus comorbid was significantly associated with the incidence of death in COVID-19 patients. The results of the study are supported by the research of Yan et al. (2020), which shows that there is a significant relationship between comorbid diabetes mellitus and the incidence of death in COVID-19 patients. Someone who has diabetes mellitus comorbid will increase the risk of death 4,77 times greater than someone who does not have diabetes mellitus comorbid. People with diabetes mellitus have elevated levels of purines in the blood. Purines can trigger the entry of the SARS-CoV 2 virus into host target cells, so people with diabetes mellitus are more at risk for infection with COVID-19 (Ganesan, Venkatratnam, Mahendra, & Devarajan, 2020). Patients with diabetes mellitus also have levels of the enzyme *Angiotensin-Converting Enzyme 2* (ACE2) high in the lungs. The ACE2 enzyme becomes a binding site for the SARS-CoV 2 virus so that if the level of ACE 2 in the lungs is high, more viruses will bind and infect (Yang et al., 2020). The massive number of viruses that enter the body in patients with diabetes mellitus causes complications in the respiratory system. It can cause severe conditions and death due to lung damage, septic shock, *Acute Respiratory Distress Syndrome* (ARDS), kidney failure, and heart failure (Riddle et al., 2020).

Relationship of Hypertension Comorbid with Death in COVID-19 Patients

This study indicates that hypertension comorbidity does not significantly correlate with the incidence of death in COVID-19 patients. The results of the study are in line with the research of Satria, Tutupoho, & Chalidyanto (2020), which said that there was no significant relationship between hypertension comorbid and death in COVID-19 patients. However, the results of this study were different from the study of Lippi, Wong, & Henry (2020) which showed there is a significant relationship between hypertension comorbid and the incidence of death in COVID-19 patients. Someone who has hypertension comorbid will increase the risk of death 2,42 times greater than someone who does not have comorbid hypertension.

Hypertension is one of the comorbidities that can cause various complications of diseases such as coronary heart disease, diabetes mellitus, stroke, and other cardiovascular diseases. Various complications caused by chronic hypertension result in a compromised immune system, so it can be at risk for infection with COVID-19 causing severity and even death (Zaki, Alashwal, & Ibrahim, 2020). Uncontrolled hypertension comorbidities can affect the development of the COVID-19 patient's condition to be severe and at high risk of death. Researchers have shown an increase in blood pressure and an increase in *Acute Respiratory Distress Syndrome* (ARDS), respiratory failure, septic shock, ICU admission, and death (Chen et al., 2020). Patients with hypertension require monitoring and intensive care so that it does not develop into a severe condition and lead to death. The difference in the study results could be due to the small number of cases of hypertension in COVID-19 patients reported at the Lamongan District Health Office.

Efforts to Prevent COVID-19 Death

The results of the study show that old age and diabetes comorbid can be at significant risk of death. Individuals in the old age group who have comorbidities are at great risk of death, so they need special attention (Siagian, 2020). Understanding and knowledge of groups at high risk of death can be an effort to prevent COVID-19 deaths. It can raise awareness for more protection in control of ourselves and our family from being infected COVID-19 and even death. Controlling comorbidities suffered by individuals can reduce the potential for being infected with COVID-19 and experiencing death.

Research Limitations

A limitation of this study is that the characteristics of the symptoms suffered by the patients were not studied due to limited data sources.

CONCLUSION

The majority of COVID-19 patients in Lamongan Regency are more than 60 years old and male. Age and diabetes mellitus comorbid have a significant relationship with mortality in COVID-19 patients in Lamongan Regency. Gender and hypertension comorbid did not significantly correlate with mortality in COVID-19 patients in Lamongan District.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest in this study.

RESEARCHERS CONTRIBUTION

YNN and ACH contributed equally to the preparation and final approval of this study. YNN took part in conceptualization, methodology, drafting, statistical analysis, and data interpretation. ACH took part in reviewing, revising, and overseeing the drafting of the manuscript. All authors have agreed to the writing and order of the manuscript.

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