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Article

The Relationship Between Diabetes Mellitus and Oxygen Saturation Levels by Pulse Oximetry in COVID-19 Inpatient at RS PKU Muhammadiyah Bantul in 2020 – 2022

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ABSTRACT

The number of Coronavirus Disease 2019 (COVID-19) patiens who have Diabetes Mellitus (DM) comorbidities in Yogyakarta Province is quite high (37.3%). Diabetes Mellitus comorbidities are thought to increase the severity of symptoms that appear in COVID-19 patients. Diabetes mellitus impairs the phagocytic ability of neutrophil white blood cells, chemotaxis, and the destruction of microorganisms within the cells. Therefore, COVID-19 patients with comorbid diabetes mellitus exhibit lower oxygen saturation levels. This study aims to the relationship between DM and oxygen saturation levels in COVID-19 inpatients at RS PKU Muhammadiyah Bantul. This research is a case control study with secondary data. The total number of respondents in this study was 144 samples consisting of COVID-19 patients with DM (n=72) and COVID-19 patients without DM (n=72). Univariate analysis with 72 case groups (DM groups) showed that the majority of the samples were male (51.4%). The age range of the case group (DM groups) was mainly in the age range of 50-59 years (51.45%) with the most frequent symptoms being fever, headache, and myalgia (45.8%). Desaturation occurred in most of the case groups (DM groups) (63.9%). Bivariate analysis using the chisquare test showed that there was a significant relationship between DM and oxygen saturation levels in COVID-19 inpatients. COVID-19 patients with DM are four times more at risk of desaturation than non-DM patients (p value = 0.000; OR = 4.021). More desaturation events at RS PKU Muhammadiyah Bantul were experienced by men, aged 50-59 years, and experiencing symptoms of fever.

Keywords: COVID-19; Diabetes Mellitus; Oxygen Saturation; Pulse Oximetry

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by blood sugar levels that exceed normal values due to abnormalities in insulin function, insulin secretion, or both[1]. The number of DM patients in Indonesia increased from 6.9% in 2013 to 8.5% in 2018[2]. Special Region of Yogyakarta (DIY), Jakarta, North Sulawesi, and East Kalimantan are the four provinces with the highest prevalence in Indonesia in 2013 and 2018. Diabetes mellitus a factor that complicates several diseases, including Coronavirus Disease 2019 (COVID-19)[3].

COVID-19 is a disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and is considered a new betacoronavirus that infects humans[4]. In Indonesia, COVID-19 cases have been increasing since late January 2022 due to the emergence of a new variant, the omicron variant. On February 16, 2022, there were 64,718 daily confirmed COVID-19 cases in Indonesia[5]. As for the total confirmed cases in the Special Region of Yogyakarta (DIY) since March 2022, there were 220,613 cases, with a death toll reaching 5,899. Bantul District became the second district in DIY with the highest death toll, totaling 88 people[6].

COVID-19 patients with comorbid DM will develop more severe clinical manifestations and also have increased mortality rates. Additionally, diabetes patients with COVID-19 are twice as likely to develop more severe COVID-19 disease and twice as likely to die. Patients with DM who suffer from COVID-19 have a greater risk of developing acute respiratory distress syndrome (ARDS) and require more complex care[7].

Viral clearance in patients with diabetes takes a longer time[8]. This occurs due to elevated blood glucose levels, which weaken the patient's immune system[9]. In COVID-19 patients with comorbid DM, there is an increase in serum biomarkers related to inflammation, such as interleukin-6 (IL-6), D-dimer, C-reactive protein (CRP), serum ferritin, and coagulation indices[8]. Increased fibrinogen, D-dimer, and CRP in DM patients can lead to a hypercoagulable state in COVID-19 patients. COVID-19 patients with comorbid DM exhibit worse inflammatory responses and pulmonary infiltration, as indicated by increased levels of neutrophils, blood urea nitrogen, total bilirubin, cardiac troponin I, procalcitonin, and decreased albumin levels[10].

Chronic diseases such as DM is a risk factor that cause COVID-19 patients experience high rates of morbidity and high mortality. DM patients are more likely to be malnourished and prone to developing cytokine storms, which can eventually lead to rapid deterioration, than non-DM patients. Hyperglycemia in DM can enhance the replication of SARS-CoV-2[11]. SARS-CoV-2 damages immune cells and increases apoptosis in CD3, CD4, and CD8 T lymphocytes, contributing to a decrease in lymphocyte count. Diabetes mellitus impairs the phagocytic ability of neutrophils, as well as chemotaxis and the destruction of microorganisms within cells. Therefore, COVID-19 patients with comorbid diabetes mellitus exhibit lower oxygen saturation levels[12]. Another study reported that hyperglycemia-induced cellular hypoxia and mtROS may promote hyperglycemic damage in a coordinated manner. A recent study has shown an elevated ACE2 expression, and its glycated product, in COVID-19 patients who had hyperglycemia. This study has also reported that COVID-19 patients with sustained hyperglycemia had low oxygen saturation levels. In summary, hyperglycemia is one of the critical factors contributing to the low oxygen saturation levels

observed in diabetic individuals, and is responsible for various exacerbations reported in diabetic individuals suffering from COVID-19 levels[10].

In the Special Region of Yogyakarta (DIY), COVID-19 cases with comorbid diabetes mellitus (DM) account for 37.3% of all comorbid conditions in confirmed COVID-19 patients. This makes DM the second most common comorbidity associated with COVID-19, following hypertension. Diabetes mellitus ranks first with a percentage of 13.7% as a comorbidity in COVID-19 patient mortality[13]. Based on this background, research is needed to determine the relationship between diabetes mellitus and oxygen saturation levels in COVID-19 patients treated at PKU Muhammadiyah Hospital in Bantul[6].

METHODS

This study is an analytical observational research with a case-control design aimed at exploring the relationship between diabetes mellitus and oxygen saturation levels in hospitalized COVID-19 patients at PKU Muhammadiyah Bantul Hospital. This study was approved by the health research ethics committee of PKU Muhammadiyah Bantul Hospital (046/EC.KEPK/C/02.23) and has received permission from the PKU Muhammadiyah Bantul Hospital (0554/KET/B/02.23). The population for this study includes all COVID-19 patients, both with and without DM, who were hospitalized at PKU Muhammadiyah Hospital from January 1, 2020, to December 31, 2022. The case group includes inpatients aged 20-79 years at PKU Muhammadiyah Hospital (2020-2022) diagnosed with COVID-19 and diabetes mellitus. The control group consisted of male and female COVID-19 patients aged 20-79 years who were hospitalized at PKU Muhammadiyah Bantul Hospital during the same period and were not diagnosed with diabetes mellitus. The exclusion criteria for this study include patients COVID-19 with comorbidities such as hypertension, COPD, CHF, and CKD, as well as those with incomplete medical records, such as missing age or SpO2 data, or unreadable medical records. The sampling technique used is purposive sampling.

This study is a retrospective analysis using data sourced from secondary data from medical records of patients who were previously hospitalized at PKU Muhammadiyah Hospital in Bantul. The variables in this study are COVID-19 with diabetes mellitus as the independent variable, while oxygen saturation is the dependent variable. Data were analyzed using SPSS (Statistical Product and Service Solutions) version 21. Univariate analysis was conducted to determine the frequency distribution (N) and percentage (%) displayed in a frequency distribution table. In the bivariate analysis, data were analyzed using the chi-square test. A

relationship is considered significant if $p < 0.05$. To estimate the risk of outcomes due to the presence of the independent variable, odds ratio (OR) was used.

RESULTS

During the study period from February to April 2023, based on the sampling technique using quota sampling, the number of subjects who met the inclusion and exclusion criteria for the case group was 72 samples, and the control group also consisted of 72 samples. The characteristics of the case and control groups at PKU Muhammadiyah Hospital in Bantul can be seen in Table 1.

***Table 1**. Frequency Distribution of Respondent Characteristics*

Frequency Distribution	*Case (DM)*		*Control (Not a DM)*	
	Frequency (N=72)	*Percentage (%)*	*Frequency (N=72)*	*Percentage (%)*
Gender				
Female	35	48.6	32	44.4
Male	37	51.4	40	55.6
Age				
20-29 years old	0	0.0	0	0.0
30-39 years old	5	6.9	72	100.0
40-49 years old	25	34.7	0	0.0
50-59 years old	37	51.4	0	0.0
60-69 years old	1	1.4	0	0.0
70-79 years old	4	5.6	0	0.0
Symptom				
Respiratory symptoms	28	38.9	30	41.7
Gastrointestinal symptoms	11	15.3	14	19.4
Other symptoms	33	45.8	28	38.9
Saturation				
Normal	26	36.1	50	69.4
Desaturation	46	63.9	22	30.6
The degree of COVID-19				
Asymptomatic	0	0.0	0	0.0
Mild	0	0.0	0	0.0
Moderate	26	36.1	51	70.8
Severe	26	36.1	13	18.1
Critical	20	27.8	8	11.1
Total	**72**	**100.0**	**72**	**100.0**

The characteristics of the case and control groups in this study include gender, age, symptoms, saturation, and severity of COVID-19. The data showed that in the case group of COVID-19 patients with comorbid diabetes mellitus, the prevalence of males was higher (n=37; 51.4%) compared to females (n=35; 48.6%). In the control group of COVID-19 patients without diabetes mellitus, the prevalence of males was also higher (n=40; 55.6%) compared to females (n=32; 44.4%). The age range of COVID-19 cases with comorbid diabetes mellitus was primarily in the

50-59 year range (n=37; 51.4%), while in the control group, all subjects were in the 30-39 year range (n=72; 100.0%).

The most frequently reported symptoms in the case group were symptoms outside the respiratory and digestive systems, such as fever, headache, and myalgia (n=33; 45.8%). There were 28 samples (38.9%) that experienced respiratory symptoms, including cough, runny nose, sore throat, shortness of breath, and anosmia. Additionally, 11 samples (15.3%) experienced gastrointestinal symptoms, such as nausea, vomiting, abdominal pain, and diarrhea. In contrast, the most common symptoms in the control group were respiratory symptoms (n=30; 41.7%). The decrease in oxygen saturation in the case group occurred in 46 samples (63.9%), while 26 samples (36.1%) had normal saturation. In the control group, 50 samples (69.4%) had normal saturation, while 22 samples (30.6%) experienced decreased oxygen saturation.

Table 2. *Frequency Distribution of Respondent Characteristics*

DM	***Saturation***				***Total***		***P value***	***OR***
	Normal		***Desaturation***					
	N	***%***	***N***	***%***	***N***	***%***		
Not a DM	50	34.7	22	15.3	72	50.0		
DM	26	18.1	46	31.9	72	50.0	0.000	4.021
Total	76	52.8	68	47.2	144	100.0		

Among COVID-19 patients without diabetes mellitus (DM), 50 samples (34.7%) had normal saturation, while 26 samples (18.1%) of COVID-19 patients with DM had normal saturation. COVID-19 patients without DM who experienced desaturation numbered 22 samples (15.3%), whereas 46 samples (31.9%) of COVID-19 patients with DM experienced desaturation. Bivariate analysis in this study was conducted using the chi-square test, yielding a p-value of 0.000 and an odds ratio (OR) of 4.021 (see Table 2). There is a significant relationship between DM and oxygen saturation levels in hospitalized COVID-19 patients. COVID-19 patients with DM are four times more at risk of experiencing desaturation compared to patients without DM (OR=4.021).

DISCUSSION

This study was dominated by males, accounting for 51.4%. This is consistent with research by Yan (2020) at Tongji Hospital in Wuhan, which found that 68.8% of COVID-19 samples with diabetes mellitus (DM) were male[14]. The study conducted by Karya (2021) also found that males with comorbid DM are more likely to experience COVID-19 compared to females[15]. It is known that females have protective factors from estrogen and progesterone and possess a better immune

system compared to males. In males, the number of B cells decreases, leading to reduced antibody production by B lymphocytes. A lack of antibodies can weaken an individual's ability to fight against the SARS-CoV-2 virus[16].

The frequency distribution data for age shows that the majority of COVID-19 patients with DM are over 50 years old, particularly in the 50-59 age range (n=37; 51.4%). This aligns with research conducted by Hadian (2022) and Alshukry (2020), which reported that the majority of COVID-19 patients are over 50 years old[17,18]. A study by Dudley (2020) stated that the highest number of COVID-19 cases is found in the 50-59 age range[19]. The prevalence of COVID-19 among patients over 50 years is attributed to a decline in the immune system as individuals age. The immune function has been shown to experience dysregulation, leading to an increased risk of infection with the SARS-CoV-2 virus. This process of weakening immune function is referred to as immunosenescence[20]. Lynch (2021) in his study revealed that aging is associated with a decrease in the number of B cells and T cells, such as CD4+ and CD8+ T cells, which are early indicators of severity in COVID-19 patients[21].

The frequency distribution data for symptoms (Table 1) shows that 33 patients (45.8%) experienced symptoms outside of the respiratory and digestive systems, such as fever, headache, and myalgia, which were the most common symptoms reported in this study. The next most common symptoms were respiratory symptoms, including cough, runny nose, sore throat, shortness of breath, and anosmia, experienced by 28 patients (38.9%), followed by gastrointestinal symptoms such as nausea, vomiting, abdominal pain, and diarrhea reported by 11 patients (15.3%). This is consistent with research by Putri (2021), which reported that the gastrointestinal symptoms in COVID-19 confirmed patients such as abdominal pain, diarrhea, nausea, vomiting, constipation, and melena. ACE2, as the receptor of S protein, was found abundantly in intestinal enterocytes besides in the respiratory system. En-terocyte abnormality induces decreased absorption of NA+, water, and mucosal disaccharides. It leads to in-creased undigested mono and disaccharides, carbohydrates, fats, and protein into the colon. As a result, the colon is unable to absorb sufficient water, leading to diarrhea. [22]. This contrasts with the cross-sectional study conducted by Siregar (2019), which showed that shortness of breath was the most prevalent symptom, affecting 137 patients (82%), followed by fever in 119 patients (71%) and diarrhea in 108 patients (65%)[20]. Shortness of breath perception in COVID-19 may be explained by two mechanisms; the direct invasion of SARS-CoV-2 to ACE2 expressing brain cells in the limbic system (especially the insular area), or by the indirect toxic effect of cytokine storm in the corticolimbic network that has the main role in expressing the perception of shortness of breath[20].

The frequency distribution data for saturation (Table 1) shows that 26 patients (36.1%) had normal saturation, while 46 patients (63.9%) experienced desaturation. This is consistent with the research by Ustun (2021), which indicated that among 66 COVID-19 patients, 46 patients with DM experienced desaturation, with an average saturation of 63.80[23]. Desaturation in COVID-19 patients can be caused by various factors, such as the immune system and the presence of comorbidities that patients had prior to contracting COVID-19, one of which is diabetes mellitus. The immune system in COVID-19 patients shows a decline, particularly in T lymphocytes and B lymphocytes[24]. Similar results were also found in a study conducted by Li (2020). The research carried out at the Wuhan Red Cross Hospital in China with 76 samples found that COVID-19 patients with comorbid diabetes mellitus had lower oxygen saturation ($P \leq 0.001$). The study also compared cases with a control group, where the case group had a lower range of oxygen saturation, ranging from 93-97%, compared to the normal oxygen saturation levels of 95-98% in COVID-19 patients without diabetes mellitus[25].

Chronic diseases such as DM is a risk factor that cause COVID-19 patients experience high rates of morbidity and high mortality. DM patients are more likely to be malnourished and prone to developing cytokine storms, which can eventually lead to rapid deterioration, than non-DM patients. Hyperglycemia in DM can enhance the replication of SARS-CoV-2[11]. SARS-CoV-2 damages immune cells and increases apoptosis in CD3, CD4, and CD8 T lymphocytes, contributing to a decrease in lymphocyte count. Diabetes mellitus impairs the phagocytic ability of neutrophils, as well as chemotaxis and the destruction of microorganisms within cells. Therefore, COVID-19 patients with comorbid diabetes mellitus exhibit lower oxygen saturation levels[12]. Another study reported that hyperglycemia-induced cellular hypoxia and mtROS may promote hyperglycemic damage in a coordinated manner. A recent study has shown an elevated ACE2 expression, and its glycated product, in COVID-19 patients who had hyperglycemia. This study has also reported that COVID-19 patients with sustained hyperglycemia had low oxygen saturation levels. In summary, hyperglycemia is one of the critical factors contributing to the low oxygen saturation levels observed in diabetic individuals, and is responsible for various exacerbations reported in diabetic individuals suffering from COVID-19 levels[10].

CONCLUSION

In this study, it can be concluded that desaturation is more commonly experienced by male patients aged 50-59 years who exhibit symptoms of fever. The study indicates a significant relationship between DM and oxygen saturation levels in hospitalized COVID-19 patients, showing

that COVID-19 patients with DM are four times more likely to experience desaturation compared to non-DM patients. Further research is needed with a larger sample size, more diverse data, and an extended timeframe to enhance the reliability of the findings and better represent the population in the Special Region of Yogyakarta (DIY).

ETHICAL APPROVAL

The study obtained ethical approval with approval number 046/EC.KEPK/C/02.23 from PKU Muhammadiyah Bantul Hospital.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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