

Research Article

Characteristics and Outcomes of COVID-19 Patients with Diabetes Mellitus at the University of Muhammadiyah Malang General Hospital

Ro'di Nur Fajri^{1*}, Ardhi Bustami¹, Zata Dini¹, Dinda Amalia Eka Putri², and Anggita Puspitasari²

¹University of Muhammadiyah Malang General Hospital

²Medical Faculty University of Muhammadiyah Malang

ORCID

Ro'di Nur Fajri: <https://orcid.org/0000-0001-7752-9066>

Abstract.

The number of confirmed cases of COVID-19 in East Java is 590,531 (9,41% of total national confirmed cases). The death toll in the province is 31,774. Diabetes Mellitus (DM) can cause systemic complications such that COVID-19 patients with DM have a high risk of serious illness and mortality. The characteristics and outcomes of COVID-19 patients with DM at the University of Muhammadiyah Malang General Hospital have never been reported before. Data were taken from medical records at the University of Muhammadiyah Malang General Hospital. The diagnosis of COVID-19 was obtained from a positive PCR swab. DM diagnosis was made by studying the patient history of DM or Random Blood Glucose (RBG) >200 mg/dL or HbA1c >7% sampling. Characteristics of the patients were age, gender, length of treatment, history of DM, and adherence to DM control. The supporting examinations were leukocytes, platelets, O₂ saturation, RBG, HbA1c, CRP, and *D-dimer*, which were grouped into two groups: recovered and dead. Data were analyzed with the SPSS version 28. COVID-19 patients with DM from June 2020 to May 2021 were 206 (23.09%) out of 892 confirmed COVID-19. The majority of cases occurred in men (51.5%) and occurred in the age range of 51-60 years (38.3%). The number of patients who died was 38 (18.4%). The average platelet value was 286,191, the average leukocyte value was 7804, the average oxygen saturation was 90%, the average HbA1c value was 9.4%, the average CRP value was 68.99mg/L, and the average D-dimer value is 13,39ng/mL. There was a significant difference in oxygen saturation and D-Dimer between recovered and dead patients. There were no significant differences in the results of other investigations.

Keywords: COVID-19, DM, mortality, University of Muhammadiyah Malang General Hospital

Corresponding Author: Ro'di Nur Fajri; email: rodinurfajri19@gmail.com

Published 8 March 2023

Publishing services provided by Knowledge E

© Ro'di Nur Fajri et al. This article is distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use and redistribution provided that the original author and source are credited.

Selection and Peer-review under the responsibility of the ICMEDH Conference Committee.

OPEN ACCESS

1. INTRODUCTION

At the end of December 2019, a case of pneumonia caused by *Novel Coronavirus infection* occurred in Wuhan, Hubei province, China and quickly spread to various other countries in the world(1). This type of coronavirus is named *Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)* and the disease caused by SARS-CoV2 is called *Coronavirus Disease-2019 (COVID-19)*(2). The first case of COVID-19 in Indonesia was discovered in early March 2020. Until August 2022, there are 6,273,228 confirmed cases in Indonesia and 157,189 patients died (2,5% of the total confirmed cases)(3). the number of cases in East Java is 590,531 (9,41% of the total national confirmed cases). The number of dead cases in East Java province is 31,693 with a Case Fatality Rate (CFR) of 5.36%(4).

Diabetes Mellitus (DM) is a common metabolic disorder, characterized by hyperglycemia caused by absolute or relative deficiency of insulin secretion and/or insulin action(5). Based on data obtained from the Indonesian Central Statistics Agency in 2003, it is estimated that the prevalence of DM in 2030 will be 194 million people aged over 20 years. Result report from Basic Health Research (RISKESDAS) 2018 by the Ministry of Health an increase in the prevalence of DM to 8.5%(6). DM is one of the chronic diseases that most common causes of multi-systemic complications. Patients with DM who suffer from COVID-19 have a risk of severe disease course and a high risk of mortality. Several studies have reported an association between severe COVID-19 infection and DM. Several factors, especially a compromised immune system, a high inflammatory response, and hypercoagulable conditions contribute to an increase in the severity of the disease(7,8).

Data regarding the outcome of COVID-19 patients with comorbid DM have not been widely reported in Indonesia. We report and observe the characteristics and outcomes of COVID-19 patients with DM at the University of Muhammadiyah Malang General Hospital during June to November 2020.

2. MATERIALS AND METHODS

Retrospective research was conducted on medical record data of COVID-19 patients with DM who were treated in the COVID-19 Isolation Room of at University of Muhammadiyah Malang General Hospital during June 2020 to May 2021. Patients who were included in the data analysis were confirmed COVID-19 patients with DM. The diagnosis

of COVID-19 was confirmed by a *Reverse transcriptase polymerase chain reaction* (RT-PCR) examination on positive nasopharyngeal and oropharyngeal swabs. The diagnosis of DM is based on a history of previous medical history (RPD), and/or the results of the Random Blood Glucose (RBG) examination > 200 or HbA1c >7 . The characteristics of the patients observed were age, gender, length of treatment. The results of the investigations that were checked at the time of initial admission to the hospital were levels of Leukocytes, Platelets, O₂ saturation when the patient arrived at the hospital, RBG, HbA1c, *C-Reactive Protein* (CRP), and *d-dimer*. The results of the examination were compared between the group of patients who recovered and the group of patients who died. Data analysis was performed using Statistical Package for Social Sciences (SPSS) software version 28.

3. RESULTS

The number of confirmed COVID-19 patients being treated in the COVID-19 isolation room at the University of Muhammadiyah Malang during the period June 2020 to May 2021 is 892. Meanwhile, the number of patients suffering from DM is 206 (23,09%). Male patients are 106 (51,5%) and female patients are 100 (48,5%). Patients vary in age, the youngest is 21 years old and the oldest is 84 years old. Cases of death obtained in COVID-19 patients with DM are 38 (18,4%). The number of patients who are declared recovered and discharged is 168 (81,6%).

Supportive examination data such as Leukocyte, Platelet, HbA1c, CRP, and *D-dimer* levels are not obtained completely in all patients. Supporting examination data displays in the form of overall average and the average for each group of outcomes (the group of recovered patients and the group of patients who died) to make it easier to see the general picture and comparison of the two groups.

There is a statistically significant difference in the average value of leukocytes ($p=0,023$). However, the average value of leukocytes in both groups is still considered normal (7,638 and 7,571). There is no statistically significant difference in the average value of platelets, ($p=0,577$). The average value of platelets from the two groups there is not much different (251,222 and 285,131). Most of the patients come to the ED with a decrease in oxygen saturation of 91%. The group of patients who died have a lower oxygen saturation than the patients who recovered are 90% and 91%. There is a significant difference in the average value of oxygen saturation statistically ($p<0,001$). On examination of RBG and HbA1c, there is no statistically significant average value in both groups ($p = 0,373$ and $p = 0,978$). In general, RBG levels in all recovered and

TABLE 1: Characteristics of COVID-19 Patients with DM.

Variable		Total (%)
Number of patients	June 2020	3 (1,5%)
	July 2020	9 (4,4%)
	August 2020	17 (8,3%)
	September 2020	9 (4,4%)
	October 2020	20 (9,7%)
	November 2020	13 (6,3%)
	December 2020	48 (23,3%)
	January 2021	24 (11,7%)
	February 2021	16 (7,8%)
	March 2021	19 (9,2%)
	April 2021	16 (7,8%)
	May 2021	12 (5,8%)
Age	21-30	2 (1%)
	31-40	10 (4,9%)
	41-50	35 (17%)
	51-60	79 (38,3%)
	61-70	50 (24,3%)
	>70	30 (14,6%)
Gender	Male	106 (51,5%)
	Female	100 (48,5%)
Treatment time	≤10 days	135 (65,5%)
	>10 days	71 (34,5%)
Previous DM history	Exist	131 (63,6%)
	Not	75 (36,4%)
DM control compliance	DM control routine	87 (42,2%)
	Not Controlled DM	119 (57,8%)
Discharge Condition	Healed	168 (81,6%)
	Died	38 (18,4%)

dead patients are beyond normal at 260 mg/dL. HbA1c levels in COVID-19 patients are also very high at 9,57%. In general, RBG levels in all recovered and dead patients are beyond normal at 260 mg/dL. HbA1c levels in COVID-19 patients are also very high at 9,57%, and the HbA1c value shows the patient's daily average RBG range is >250 mg/dL.

CRP value increases in almost all COVID-19 patients with DM. On CRP examination, there is a difference in the average of patients who recovered and died. The average value of CRP in patients who died is 78,18 mg/L, while the average value of CRP in patients who recovered is 75,11 mg/L. Statistically, the average value of CRP of the two groups is not significantly different ($p=0,97$). On examination of D-dimer shows an

TABLE 2: Examination Results for COVID-19 Patients with DM in each group.

Variable	Total	Average	Minimum value	Maximum value	p value
Leukocytes Died Recovered	204	7,579	2,910	21,650	0.023
	37	7,638	4,350	21,650	
	167	7,571	2,910	20,180	
Platelets Died Recovered	204	280.771	76.000	837.000	0.577
	37	251.222	10.8000	658.000	
	167	285.131	76.000	837.000	
Oxygen Saturation Died Recovered	206	91%	36%	98%	<0.001
	38	90%	58%	98%	
	168	91%	36%	98%	
RBG Died Recovered	206	260	55	1,264	0.356
	38	289	126	858	
	168	256	55	1,264	
HbA1C Died Recovered	172	9,57	5,2	14	0.473
	26	9,38	6,8	13,9	
	146	9,59	5,2	14	
CRP Died Recovered	185	75,50	2,19	200	0.97
	32	78,19	11,41	200	
	153	75,11	2,19	200	
D-Dimer Died Recovered	177	2,89	0,2	51,45	0.018
	30	5,58	0,2	51,45	
	147	2,50	0,2	50	

increase in almost all patients. The average value of D-dimer in COVID-19 patients with DM is 2,89. The average value on the D-dimer in patients who died was higher than in patients who recovered, 5,58 and 2,50. Statistically, the average value of D-dimer of the two groups is significantly different ($p= 0,018$).

4. DISCUSSION

The results of the medical records of University of Muhammadiyah Malang General Hospital proved that there were more male COVID-19 patients with DM than female COVID-19 patients with DM (106 versus 100). The most cases of COVID-19 with DM at the University of Muhammadiyah Malang General Hospital were in the age group above

51-60 years. Older men are epidemiologically associated with the prevalence of COVID-19 with severe symptoms. Other studies have confirmed that men and increasing age have been associated with worse outcomes(9). The potential of worsening of COVID-19 infection with DM may increase in the elderly. This is probably due to a decrease in the function of T cells and B cells at the elderly, causing a general decline in the immune system(10).

The average value of leukocytes and platelets in this study does not seem much different between the two groups. Most COVID-19 patients usually have normal or reduced leukocyte values¹⁰. The increase in leukocyte levels may be caused by a secondary infection by bacteria. Some COVID-19 patients with DM have decreased platelet value. This may be caused by two mechanisms, a decrease in the number of megakaryocytes and an increase in the use of platelets. Lungs are organs capable of maturation of megakaryocytes, with lung damage in COVID-19 patients, platelet levels will decrease(11). Damage to the lung tissue can also lead to activation, aggregation and retention of platelets in the lung, and can also lead to thrombus formation in the injured area, which will lead to a reduction in the number of platelets due to overuse(12).

Most of the COVID-19 patients with DM come to ER at at University of Muhammadiyah Malang General Hospital with decreased oxygen saturation. Almost patients who died come with low oxygen saturation conditions had an average oxygen saturation value of 90%. On the other hand, patients who come with stable oxygen saturation and with mild to moderate symptoms are almost entirely discharged from the hospital in good condition. The condition of decreased oxygen saturation in COVID-19 is known as *happy hypoxia*. *Happy hypoxia* is a condition where the patient seems to be breathing normally. There is no difficulty in breathing or feeling of discomfort when breathing, but oxygen saturation levels have decreased(13). This causes most of the patients to feel fine and come to the ER late due to severe desaturation.

This is in line with several other studies showing that SpO₂ <90% has 1.86-7.74 times of risk of death compared to saturation >90%(14). This is supported by other studies with SpO₂ <95% having a risk of death 2.81 to 8.81 times higher than SpO₂ >95%. In a study that correlated hypoxia with patient outcome, it was found that every one percent increase in oxygen saturation reduced the risk of death by up to 8%. In the same study, it is also stated that if the SpO₂ < 90%, there was a strong risk of death. (15) Hypoxic conditions describe poor lung function and low oxygen levels. The detection of oxygen saturation is very important in recognizing the early symptoms of ARDS. So, if poor oxygen saturation is found, appropriate interventions can be immediately conducted. So that it can reduce the incidence of ARDS and the risk of death in patients.

Patients with hypoxemia will cause various cytotoxic conditions in neutrophils and cause hyperinflammation.(14)

Examination of RBG levels is very important for initial screening in the ER because it can increase the doctor's alertness to decide whether the patient is a DM patient or not because not all DM patients are aware that they are suffering from DM. It can be proven that from 206 COVID-19 patients with DM, 75 (36,4%) patients do not realize that they are suffering from DM. Early diagnosis of DM during treatment is very important so that patient management can be conducted comprehensively.

The high average value of HbA1c in this study indicates that the majority of COVID-19 patients with DM are not well controlled. Only 87 (42,2%) patients had regular check-ups at the hospital and took medicines regularly. Control of blood glucose levels plays a big role in the prognosis of COVID-19 patients with DM. Conditions of hyperglycemia can worsen the progression of virus infections in the respiratory tract, one of them is by suppressing the immune system and increasing the production of pro-inflammatory cytokines. (16) SARS-CoV-2 infection in DM patients can also trigger stress conditions that can increase counter-insulin hormones such as glucocorticoids and catecholamines. This can worsen the condition of hyperglycemia, insulin resistance, and other complications. (17)

Almost all of the COVID-19 patients with DM have a high CRP value of 75.70. The average value of CRP obtained in the group of patients who died was higher than the group of patients who recovered, although statistically not significantly different. CRP is a protein that is induced by IL-6 during inflammation. Elevated CRP levels in COVID-19 patients with DM indicate the presence of acute inflammation. Very high levels of the inflammatory marker CRP (more than 200 mg/L) and ferritin levels of more than 2500 ng/mL are risk factors for COVID-19 with severe symptoms.(18) Cytokine storms are a significant cause of death in the development of the COVID-19 disease. Patients with CRP levels higher than 41.8 mg/L may experience more severe COVID-19 conditions than those with lower CRP levels. (14)

Examination of D-dimer levels shows a higher increase in the group of patients who died. This shows that COVID-19 patients with DM have severe coagulation disorders. Systemic coagulation is a known complication of severe infectious conditions. Hypercoagulable conditions occur due to excessive pro-inflammatory cytokine response (possibly caused by *cytokine storm*). (19) Hypercoagulable conditions characterized by an increase in D-dimer can lead to Disseminated Intravascular Coagulopathy (DIC) conditions. In contrast to the classic DIC conditions in the setting of bacterial and posttraumatic sepsis, the decrease in platelet value in COVID-19 patients is usually mild

(platelets around 100,000-150,000 μ L)(20). Coagulation disorders that occur can cause microvascular and macrovascular complications (often causing deep vein thrombosis and pulmonary embolism) which in turn will lead to an increased risk of death in COVID-19 patients.(18,19)

Study conducted by Zhang shows that D-Dimer levels above 2.0 g/mL are predictors of death in patients with COVID-19 and this number can be a threshold predictor of worse prognosis in COVID-19 patients. Virus infection will usually be followed by a dominant inflammatory response and followed by an anti-inflammatory response that is disproportionate to the inflammatory process that occurs. This can cause endothelial cell dysfunction, resulting in the formation of large amounts of thrombin. In addition, hypoxic conditions alone in patients with COVID-19 can stimulate thrombosis due to increased blood viscosity and signal transcription pathways induced by hypoxia.(21)

Mishra, et al says that patients with diabetes have higher levels of D-dimer than those without diabetes. Diabetic conditions can lead to hypercoagulable conditions and tend to have a poorer prognosis. Chronic hyperglycemic conditions can cause endothelial dysfunction and inflammation that will lead to thrombus formation. With the SARS-CoV-2 virus infection, patients with diabetes tend to have coagulopathy and have poor outcomes.(22)

In general, the results of investigations in the group of patients who died shows worse results. The average levels of oxygen and D-dimer re significantly different in the two groups, but for other examinations they are not statistically significant. This is probably due to incomplete data. At the beginning of the pandemic, not all COVID-19 patients with DM who are hospitalized in the isolation room are examined in a complete laboratory. Examinations that have not been routinized are the levels of CRP, D-dimer, and HbA1c. Through this study, it is hoped that there will be an increase in the handling of COVID-19 patients, especially COVID-19 patients with comorbid DM.

This study has several limitations. First, this study is conducted in only one center. Second, complete laboratory data are not found in some patients, and viral load is not evaluated in this study.

5. CONCLUSION

There are 23,09% cases of COVID-19 with DM at at University of Muhammadiyah Malang General Hospital from all confirmed cases of COVID-19 during June 2020 – May 2021. The mortality rate is 18,4% of the total COVID-19 patients with DM. There were

statistically significant differences in oxygen saturation and D-dimer values between the recovered and dead groups.

References

- [1] Zhou W, Ye S, Wang W, Li S, Hu Q. Clinical Features of COVID-19 Patients with Diabetes and Secondary Hyperglycemia. *J Diabetes Res.* 2020;2020(Dm).
- [2] Wu SY, Yau HS, Yu MY, Tsang HF, Chan LW, Cho WC, et al. The diagnostic methods in the COVID-19 pandemic, today and in the future [Internet]. *Expert Rev Mol Diagn.* 2020 Sep;20(9):985–93.
- [3] KEMENKES. Media Informasi Resmi Terkini Penyakit Infeksi Emerging COVID-19 [Internet]. 2022. Available from: <https://infeksiemerging.kemkes.go.id/dashboard/covid-19>
- [4] Provinsi JDI. Info Covid-19 Jawa Timur [Internet]. 2022. Available from: <https://infocovid19.jatimprov.go.id/>
- [5] Ozder A. A novel indicator predicts 2019 novel coronavirus infection in subjects with diabetes. 2020. <https://doi.org/10.1016/j.diabres.2020.108294>.
- [6] PERKENI. Pedoman Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 Dewasa di Indonesia 2019. 2019. Available from: <https://pbperkeni.or.id/wp-content/uploads/2020/07/Pedoman-Pengelolaan-DM-Tipe-2-Dewasa-di-Indonesia-eBook-PDF-1.pdf>
- [7] Gupta R, Hussain A, Misra A. Diabetes and COVID-19: evidence, current status and unanswered research questions [Internet]. *Eur J Clin Nutr.* 2020 Jun;74(6):864–70.
- [8] Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia - A systematic review, meta-analysis, and meta-regression. *Diabetes Metab Syndr.* 2020;14(4):395–403.
- [9] Matteo A, Maria CC, Michele M, Laura M, Alberto CSDP, Lancet. COVID-19 in people with diabetes: understanding the reasons for worse outcomes. 2020;782–92.
- [10] Hussain A, Bhowmik B, do Vale Moreira NC. COVID-19 and diabetes: knowledge in progress [Internet]. *Diabetes Res Clin Pract.* 2020 Apr;162:108142.
- [11] Poon TC, Pang RT, Chan KC, Lee NL, Chiu RW, Tong YK, et al. Proteomic analysis reveals platelet factor 4 and beta-thromboglobulin as prognostic markers in severe acute respiratory syndrome. *Electrophoresis.* 2012 Jul;33(12):1894–900.
- [12] Pilaczyńska-Cemel M, Gołda R, Dąbrowska A, Przybylski G. Analysis of the level of selected parameters of inflammation, circulating immune complexes, and related

- indicators (neutrophil/lymphocyte, platelet/lymphocyte, CRP/CIC) in patients with obstructive diseases. *Cent Eur J Immunol*. 2019;44(3):292–8.
- [13] Konyala V, Bhat R. The Mystery of Hypoxia in COVID-19. *Int J Surg Med*. 2020;2(0):1.
- [14] Mejía F, Medina C, Cornejo E, Morello E, Vásquez S, Alave J, et al. Oxygen saturation as a predictor of mortality in hospitalized adult patients with COVID-19 in a public hospital in Lima, Peru. *PLoS One*. 2020;15:1–12.
- [15] Xie J, Covassin N, Fan Z, Singh P, Gao W, Li G, et al. Association Between Hypoxemia and Mortality in Patients With COVID-19 [Internet]. *Mayo Clin Proc*. 2020 Jun;95(6):1138–47.
- [16] Raoufi M, Khalili S, Mansouri M, Mahdavi A, Khalili N. Well-controlled vs poorly-controlled diabetes in patients with COVID-19: are there any differences in outcomes and imaging findings? [Internet]. *Diabetes Res Clin Pract*. 2020 Aug;166:108286.
- [17] Albuлесcu R, Dima SO, Florea IR, Lixandru D, Serban AM, Aspritoiu VM, et al. COVID-19 and diabetes mellitus: unraveling the hypotheses that worsen the prognosis (Review) [Review]. *Exp Ther Med*. 2020 Dec;20(6):194.
- [18] Lim S, Bae JH, Kwon HS, Nauck MA. COVID-19 and diabetes mellitus: from pathophysiology to clinical management [Internet]. *Nat Rev Endocrinol*. 2021 Jan;17(1):11–30.
- [19] Erener S. Diabetes, infection risk and COVID-19 [Internet]. *Mol Metab*. 2020 Sep;39(June):101044.
- [20] Wool GD, Miller JL. The Impact of COVID-19 Disease on Platelets and Coagulation. *Pathobiology*. 2021;88(1):15–27.
- [21] Soni M, Gopalakrishnan R, Vaishya R, Prabu P. D-dimer level is a useful predictor for mortality in patients with COVID-19: Analysis of 483 cases. *Diabetes Metab Syndr*. 2020 Nov-Dec;14(6):2245–2249. doi: 10.1016/j.dsx.2020.11.007.2020.
- [22] Mishra Y, Kumar B, Sourabh S. Relation of D-dimer levels of COVID-19 patients with diabetes mellitus. 2020. <https://doi.org/10.1016/j.dsx.2020.09.035>.