ORIGINAL PAPER

Factors Affecting the Outcomes of COVID-19 in Diabetes Patients at Haji Adam Malik General Hospital Medan, Indonesia

Nadya Joana Marpaung¹, Mustafa Ali Azmi Lubis¹, Rina Amelia²

¹Undergraduated Program in Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan. Indonesia

²Department of Community Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan. Indonesia

Corresponding author: Rina Amelia. Department of Community Medicine/Public Health, Faculty of Medicine, Universitas Sumatera Utara, Medan, North Sumatera, Indonesia 20155, Tel ; +628116180352. E-mail: rina2@usu.ac.id, . ORCID ID: https://orcid.org/0000-0002-0419-9622

doi: 10.5455/aim.2023.31.182-185 ACTA INFORM MED. 2023, 31(3): 182-185 Received: JUL 15, 2023 Accepted: SEP 05, 2023

© 2023 Nadya Joana Marpaung, Mustafa Ali Azmi Lubis, Rina Amelia

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/ licenses/by-nc/./) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: COVID-19 is a virulent viral infection by SARS-CoV-2 which caused pandemic and high mortality. One of the numerous risk factors for worse clinical outcomes in COVID-19 patients is the presence of comorbidity. Diabetes Mellitus is a chronic metabolic disease frequently in COVID-19 patients. Insulin resistance, causes chronic inflammation in the body, may aggravate the clinical outcome COVID-19 patients. Objective: The aim of the study was to examine factors that impact clinical outcomes in COVID-19 T2DM patients. Methods: The method used an analytical method with cross sectional design. Population is inpatients in Haji Adam Malik Hospital diagnosed with COVID-19 and Diabetes Mellitus Type 2 with 99 inpatients as sample. The data used are secondary data obtained through medical records from a hospital covering patients characteristics and laboratory result The data was analyzed using t-independent and chi square test with SPSS program. Results: Clinical outcomes for 99 patients are 60 patients are cured and 39 patients are dead. analytical study found a significant correlation between factors impacting clinical outcomes on COVID-19 patients with T2DM that are HbA1c level, D-dimer, cholesterol total and COVID-19 degree of severity and the clinical outcomes (p<0,05). Conclusion: HbA1c level, D-dimer, total cholesterol and the infection degree of severity affects the clinical outcomes on COVID-19 with T2DM (p<0,05).

Keywords: Cholesterol, COVID-19, D-dimer, Diabetes Mellitus, HbA1c, COVID-19 in Diabetes.

1. BACKGROUND

Coronavirus is one of the major families of viruses that can cause disease in both humans and animals. On December 2019 in Wuhan, China, a new type of Coronavirus was discovered which was later named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV2) and caused Coronavirus Disease-2019 (COVID-19) (1). Diabetes is a common risk factor for poor clinical outcomes in COVID-19 patients (2). Diabetes patients have been reported to have worse outcomes when infected with the COVID-19. The non-survival rate is estimated to be 22-31% higher in diabetic than in non-diabetics (3). In Indonesia, the COVID-19 mortality rate in diabetes patients is 21.28%, which is much higher than the 2.77% rate in individuals without diabetes. COVID-19 patients with DM also usually have more and severe

The COVID-19 symptoms (4). virus causes stress and stimulates the release of hyperglycemic hormones, which can lead to elevated blood sugar levels and diabetic complications (5). In diabetics, viral infections can significantly increase the inflammatory process. This can also be caused by elevated blood sugar levels, which can cause a variety of complications (6). According to laboratory results, ICU patients have increased D-dimer levels > 1 μ g/ml, greater CRP levels, and elevated LDH levels than non-ICU patients. HbA1c levels in severely patients also indicate that inadequate glycemic control can lead to poor COVID-19 infection (7).

Diabetes was associated with higher D-dimer levels compared to patients without DM, indicating a significant correlation between D-dimer levels and comorbidities with DM (8). According to research, COVID-19 infection is more severe in patients with elevated levels of TLC, D-dimer, and CRP (9).

2. OBJECTIVE

The objective of this research was to determine the factors that influence the outcomes of COVID-19 Type 2 DM patients.

3. PATIENTS AND METHODS

Study Design and ethical considerations

The analytics research design with a cross sectional design was applied to this study. The Health Research Ethics Committee of the Universitas Sumatera Utara granted authorization for the study (Number: 733/KEPK/USU/2022).

Participants

The population in this research were inpatients at Haji Adam Malik General Hospital Medan has confirmed for COVID-19 and also had Type 2 Diabetes Mellitus. Using the consecutive sampling technique, 99 samples fulfilled the criteria for inclusion and exclusion. Inclusion criteria consisted of inpatients with positive confirmation of COVID-19 with Type 2 DM and exclusion criteria were incomplete or unreadable medical record data.

Study Procedure

This study used the secondary data documentation method from the medical records of the HAM General Hospital for the period January 2021-December 2021. Analytical tests were performed to show the effect of age, gender, severity of infection, comorbidities, KGD, HbA1c, CRP, D-dimer, Ferritin, and total cholesterol levels on patient outcomes (p<0.05).

Statistical analysis

Data were analyzed using SPSS 22 Windows using the Chi-Square test and T-independent test.

4. RESULTS

COVID-19 patients with Type 2 DM are mostly between the ages of 45 and 60, with 55 people having the highest mortality rate of 21 (38.18%), followed by 35 people over 60 having a mortality rate of 14 (40.00%). The male gender is significantly larger, with 61 people, and also the highest mortality rate, with 21 people (73.43%). The most predominant degree of severity of COVID-19 infection seems to be moderate infection, which affects 45 people, followed by patients with severe infection, affect 10 people, and patients with critical infection, affect 11 patient. Severe infection had the highest mortality rate, with 22 patients (55.00%), followed by critical infection, with 11 patients (84.63%) (Table 1).

Table 1 demonstrates that 85 patients with other comorbidities have a higher mortality rate of 36 people (42.35%), whereas 14 COVID-19 patients with only Type 2 DM have a mortality rate of 3 people (21.43%). The distribution of COVID-19 comorbidities in patients with DM is known to be 85 cases (85.9%) patients with Type 2 diabetes accompanied by other comorbidities and the remaining 14 cases (14.1%) pa-

Patient Charac- teristic	Outcome				Total		
	Survive		Death		- IUIdi		p-value
	Ν	%	Ν	%	N	%	_
Age							
- Younger (<45)	5	55,56	4	44,44	9	100.00	
-Middle Age (≥45-60)	34	61,82	21	38,18	55	100.00	0,935
- Elder (>60)	21	60,00	14	40,00	35	100.00	
Sex							
- Male	40	65,57	21	73,43	61	100.00	0,200
- Female	20	52,63	18	47,37	38	100.00	
Degree of Severity							
- Mild	1	100,00	0	0	1	100.00	0,0001
- Moderate	39	86,67	6	13,33	45	100.00	
- Severe	18	45,00	22	55,00	40	100.00	
- Critical	2	15,38	11	84,62	13	100.00	
Comorbidities besid	des Type	2 Diabetes					
- Yes	49	57,65	36	42,35	85	100.00	0,138
- None	11	78,57	3	21,43	14	100.00	
Quantitative CRP-L	evels						
- Mild Elevated	39	67,24	19	32,76	58	100.00	0,108
- Moderate Ele- vated	21	51,22	20	48,78	41	100.00	
Ferritin Levels							
- Normal	4	100,00	0	0	4	100.00	— 0,100
- Abnormal	56	58,95	39	41,05	95	100.00	

Table 1. Characteristics of COVID-19 Patients with Type 2 DM

Variable	Average	n voluo		
Vallable	Survive	Death	h-vaine	
Fasting Glucose Level (mg/dL)	311,70	320,28	0,777	
HbA1c (%)	9,10	10,41	0,017	
D-dimer (mg/L)	1.465,38	2.894,23	0,003	
Cholesterol (mg/dL)	143,28	164,21	0,024	

Table 2. The average difference in variables between patients survived and death.

tients with Type 2 DM without other comorbidities. Patients with much more than one comorbidity are frequently occurring. Heart disease was the most common comorbidity, representing for 55 cases (55.6%). With 33 cases, hypertension became the most prevalent heart disease among the 55 cases, followed by Chronic heart failure, St–segment elevation myocardial, and CAD. There were 23 cases (23.2%) of High-Risk Thromboembolism, followed by cases of pulmonary diseases such as COPD, pulmonary embolism, and ARDS. There were also cases of kidney disease such as CKD and AKI, as well as 4 cases (4.04%) of DM complications such as diabetic foot ulcers and gangrene.

The laboratory results of COVID-19 patients with Type 2 DM reported that all patients had elevated quantitative CRP levels, with 58 people who are experiencing small elevations and 19 (32.76%) of them death. Twenty (48.78%) of the 41 patients who suffered from moderate elevation ended up dead. It was observed that 95 patients had elevated ferritin levels, with a mortality rate of 39 people (41.05%).

The chi-square analysis test found a significant relationship between the severity of COVID-19 infection and patient outcomes, with a p-value of 0.0001 (p0.05), but no correlation between age (0.935), gender (0.200), comorbidity (0.138), quantitative CRP levels (0.108), and ferritin levels (0100) and patient outcomes (p>0.05). The average fasting blood sugar levels was significantly high in death patients (320.28 mg/dL) than in recovered patients (311.70 mg/dL). The average HbA1c was significantly high among death patients (10.41%) than those who recovered (9.10%), the average D-dimer was significantly high among death patients (2,894.23 mg/L) than those who recovered (1,465.38 mg/L), and the average cholesterol was significantly high among death patients (164.21 mg/dL) than those who recovered (143.28 mg/dL) (Table 2).

Table 2 displays that there are differences in mean HbA1c (0.017), D-dimer (0.003), and cholesterol (0.024) levels based on patient outcomes (p0.05). Meanwhile, based on patient outcomes, there was no difference in mean fasting KGD (0.777) (p>0.05).

5. DISCUSSION

This study observed that the age group 45-60 years old has the highest COVID-19 with Type 2 DM. Of the 221 COVID-19 patients, 136 cases (61.5%) were <60 years old and the rest were \geq 60 years old (10). From 8 studies conducted in China to determine the prevalence of comorbidities of 46,248 patients infected with COVID-19, it was found that the average age of patients was 46 years (51.6%) male, with the second highest prevalence of DM after hypertension, but diabetes was associated with worse COVID-19 infection (11).

This study found that males were the most prevalent gender with COVID-19 and Type 2 DM. The Chinese CDC reported the ratio of male to female COVID-19 infection was 2.7:1 with a Case Fatality Rate (CFR) of 2.8% for males and 1.7% for females, calculated from 72,314 patients in China. It was found that the initial COVID-19 infection was worse in males, as well as indications of hospitalization and worse outcomes (12).

This study found that patients with severe and critical severity of infection had a higher mortality rate than those who recovered (p<0.05). Of the 476 COVID-19 patients, the median age was 53 years with severe and critical patients more prevalent in the older age group. The incidence of comorbidities was higher in the severe (46.3%) and critical (67.3%) groups than in the moderate infection group (37.8%)(13).

This study found that more COVID-19 patients with Type 2 DM were accompanied by other comorbidities such as heart disease (hypertension, CHF, STEMI, CAD), lung disease, high risk thrombosis and kidney disease. The study at Oujda university hospital found 188 COVID-19 patients with DM among 600 patients and 65 (34.6%) of 188 patients with DM died. Patients also suffered from other comorbidities such as hypertension, heart disease, obesity, and renal failure (14).

This study found that all patients had elevated quantitative CRP levels. Research conducted by Zhu et al. (2020) which showed that IL-6, CRP and LDH levels were significantly higher in patients with Type 2 DM and COVID-19 at re-examination at 28 days compared to patients with COVID-19 infection without Type 2 DM (15).

This study found that 97 out of 99 patients had elevated ferritin levels. Research from 99 patients by Vargas-Vargas & Cortés-Rojo found 83 patients had serum ferritin levels above normal. Laboratory test results also found that patients with severe COVID-19 infection showed a cytokine storm with elevated levels of inflammatory markers, one of which was ferritin (16).

The highest probability of death when hospitalized was found in those aged >80 years. The study conducted on 46,248 patients infected with COVID-19 also found the presence of comorbid diabetes increased mortality compared to patients who did not have comorbidities (7.3%V0.9%) (11).

This study found that the average fasting sugar levels of patients with a death outcome were higher than those with a recovery outcome. Research by Bode et al. (2020) which reported that patients treated for COVID-19 infection with diabetes or uncontrolled hyperglycemia had higher mortality rates and length of stay (17).

This study found that the average HbA1c levels of patients with a death outcome were higher than those with a recovery outcome. There was also a significant p-value calculation (p<0.05). Research on 2,068 patients infected with COVID-19 and found 183 (8.85%) patients suffering from DM. Among COVID-19 patients, many patients were found to have HbA1c levels \geq 9%. HbA1c level \geq 9% is a parameter and predictor associated with increased risk of hospitalization in COVID-19 infection (18).

This study found that the mean D-dimer level of patients with a death outcome was higher than that of patients with a recovery outcome. There was also a significant p-value calculation (p<0.05). A study at Oujda university hospital, Morocco found a significant association between D-dimer and CRP levels with diabetes. D-dimer levels > 2,885 ng/mL are predictors of mortality in COVID-19 patients with DM. The relationship between D-dimer levels in COVID-19 patients with diabetes and without diabetes showed a significant difference (p-value = 0.002) (2).

This study found that the average total cholesterol level of patients with a death outcome was higher than that of patients who recovered. There was also a significant p-value calculation (p<0.05). Zaki et al. (2020) stated that HDL-C levels were significantly lower in patients with severe and critical degrees of COVID-19 infection than in patients with mild or moderate degrees of infection. Observing serum cholesterol levels can also show improvements in the patient's condition (19).

6. CONCLUSION

To reduce mortality, it is essential to avoid diabetes as a risk factor for the poor course of COVID-19 infection. The research results show the role of HbA1c, D-dimer, total cholesterol, and infection severity on the outcome of COVID-19 patients with Type 2 DM. As a result, early detection of these factors is essential for minimizing complications and mortality.

- Patient Consent Form: All participants were informed about subject of the study.
- Acknowledgments. The authors gratefully acknowledge that the present research is supported by the Ministry of Research and Technology and Higher Education Republic Indonesia, year 2022
- Author's Contribution: RA Contributed to conception and design of the study, acquisition of data, data analysis and and drafting article. RR and SSW performed data acquisition and experimental laboratory works. HW were involved in article drafting and critically revising and

approval final version to be published. All authors have approved the final version of the manuscript

- Conflicts of interest: There are no conflicts of interest.
- Financial support and sponsorship: None.

REFERENCES

- (WHO) WHO. Coronavirus Disease (COVID-19) [Internet].
 2021 [cited 2022 Mar 10]. Available from: https://www.who.int/ health-topics/coronavirus#tab=tab_1
- Nassar M, Daoud A, Nso N, Medina L, Ghernautan V, Bhangoo H, et al. Diabetes Mellitus and COVID-19: Review Article. Diabetes Metab Syndr Clin Res Rev [Internet]. 2021 Nov; 15(6): 102268. Available from: https://linkinghub.elsevier.com/retrieve/pii/ S1871402121002885
- Cuschieri S, Grech S. COVID-19 and diabetes: The why, the what and the how. J Diabetes Complications [Internet]. 2020 Sep; 34(9): 107637. Available from: https://linkinghub.elsevier.com/ retrieve/pii/S1056872720303962
- Harbuwono DS, Handayani DOTL, Wahyuningsih ES, Supraptowati N, Ananda, Kurniawan F, et al. Impact of diabetes mellitus on COVID-19 clinical symptoms and mortality: Jakarta's COVID-19 epidemiological registry. Prim Care Diabetes [Internet]. 2022 Feb; 16(1): 65–68. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1751991821001923
- Wang A, Zhao W, Xu Z, Gu J. Timely blood glucose management for the outbreak of 2019 novel coronavirus disease (COVID-19) is urgently needed. Diabetes Res Clin Pract [Internet]. 2020 Apr; 162: 108118. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0168822720303685
- American Diabetes Association. Diabetes and COVID-19: Frequently Asked Questions [Internet]. 2022 [cited 2022 Mar 10]. Available from: https://diabetes.org/coronavirus-covid-19/ covid-19-faq
- Guo T, Shen Q, Ouyang X, Guo W, Li J, He W, et al. Clinical Findings in Diabetes Mellitus Patients with COVID-19. Cigarran S, editor. J Diabetes Res [Internet]. 2021 Jan 8; 2021: 1–7. Available from: https://www.hindawi.com/journals/jdr/2021/7830136/
- Hashim Ibrahim Elbashir I, Kamal Ali Mohamed H, Adam Essa ME, Seri A. Comparison between D-dimer levels in diabetic and non-diabetic positive <scp>COVID</scp> -19 adult patients: A hospital-based study. Endocrinol Diabetes Metab [Internet]. 2022 Jul 25; 5(4). Available from: https://onlinelibrary.wiley.com/ doi/10.1002/edm2.349
- Sharma A, Ahmad Farouk I, Lal SK. COVID-19: A Review on the Novel Coronavirus Disease Evolution, Transmission, Detection, Control and Prevention. Viruses [Internet]. 2021 Jan 29; 13(2): 202. Available from: https://www.mdpi.com/1999-4915/13/2/202

- Xiao Y-F, He J-L, Xu Y, Liu X, Lin H, Li Q, et al. Major Characteristics of Severity and Mortality in Diabetic Patients With COVID-19 and Establishment of Severity Risk Score. Front Med [Internet]. 2021 Jun 7;8. Available from: https://www.frontiersin.org/articles/10.3389/fmed.2021.655604/full
- Sinclair AJ, Abdelhafiz AH. Age, frailty and diabetes triple jeopardy for vulnerability to COVID-19 infection. EClinicalMedicine [Internet]. 2020 May; 22: 100343. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2589537020300870
- Raza HA, Sen P, Bhatti OA, Gupta L. Sex hormones, autoimmunity and gender disparity in COVID-19. Rheumatol Int [Internet].
 2021 Aug 26; 41(8):1375–1386. Available from: https://link. springer.com/10.1007/s00296-021-04873-9
- Feng Y, Ling Y, Bai T, Xie Y, Huang J, Li J, et al. COVID-19 with Different Severities: A Multicenter Study of Clinical Features. Am J Respir Crit Care Med [Internet]. 2020 Jun 1; 201(11): 1380– 1388. Available from: https://www.atsjournals.org/doi/10.1164/ rccm.202002-0445OC
- 14. Berrajaa S, Berrichi S, Bouayed Z, Mezzeoui S El, Aftiss FZ, Bkiyar H, et al. Diabetes as a predictive factor for severe form and high mortality risk of COVID-19: Retrospective cohort study of 188 cases. Ann Med Surg [Internet]. 2021 Dec; 72: 103095. Available from: https://linkinghub.elsevier.com/retrieve/pii/ S2049080121010451
- Shi Y, Wang G, Cai X, Deng J, Zheng L, Zhu H, et al. An overview of COVID-19. J Zhejiang Univ B [Internet]. 2020 May 8; 21(5): 343–360. Available from: https://link.springer.com/10.1631/ jzus.B2000083
- Vargas-Vargas M, Cortés-Rojo C. Ferritin levels and COVID-19. Rev Panam Salud Pública [Internet]. 2020 Jun 1; 44: 1. Available from: https://iris.paho.org/handle/10665.2/52235
- Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R, et al. Glycemic Characteristics and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States. J Diabetes Sci Technol [Internet]. 2020 Jul 9; 14(4): 813–821. Available from: http:// journals.sagepub.com/doi/10.1177/1932296820924469
- Merzon E, Green I, Shpigelman M, Vinker S, Raz I, Golan-Cohen A, et al. Haemoglobin A1c is a predictor of COVID-19 severity in patients with diabetes. Diabetes Metab Res Rev [Internet]. 2021 Jul 23; 37(5). Available from: https://onlinelibrary.wiley.com/ doi/10.1002/dmrr.3398
- Zaki N, Alashwal H, Ibrahim S. Association of hypertension, diabetes, stroke, cancer, kidney disease, and high-cholesterol with COVID-19 disease severity and fatality: A systematic review. Diabetes Metab Syndr Clin Res Rev [Internet]. 2020 Sep; 14(5): 1133–1142. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1871402120302514