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Comparison of Clinical Outcomes of Diabetes Mellitus Patients with COVID-19 Confirmed Diabetes Mellitus Patients at One of the Hospital Bantul

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ABSTRACT

SARS-CoV-2-infected patients with comorbid DM are very likely to experience a significant reduction in glycemic control and eventually require adjustment of antidiabetic treatment to optimize clinical outcomes. The results of data collected by the COVID-19 Handling Task Force, the total number of cases in Indonesia that were confirmed positive for COVID-19 had comorbidities, one of which was Diabetes Mellitus 33.6%. This study aimed to determine whether or not there were differences in clinical outcomes of DM patients with confirmed COVID-19 and DM without confirmed COVID-19 at One of Hospital Bantul. This type of research is observational with a cross-sectional design. Secondary data in the form of medical records. Sampling was carried out using a simple random sampling method with the Lemeshow formula. The data were analyzed using the Mann-Whitney test in bivariate analysis. The results showed that the clinical outcome of type 2 DM patients with confirmed COVID-19 was the GDS target value (38.9%) and the GDS target value (61.1%). The clinical outcome of patients with type 2 diabetes who did not have confirmed COVID-19 was that the GDS target value (55.6%) was achieved and the GDS target value was not reached (44.4%). The results of the Mann-Whitney test showed a significant difference in clinical outcome p=0.046 between DM type 2 confirmed COVID-19 and DM type 2 not confirmed COVID-19. It can be concluded that DM patients with confirmed COVID-19 have different clinical outcomes than DM patients without confirmed COVID-19.

***Keywords*:** Clinical outcomes; COVID-19; Type 2 diabetes

INTRODUCTION

Diabetes mellitus (DM) is high glucose or sugar levels in the blood plasma that exceeds normal limits, followed by typical symptoms such as polyuria (peeing a lot), polyphagia (feeling hungry straight away), polydipsia (feeling thirsty and drinking a lot) and drastic weight loss for unknown causes.[1]

COVID-19 is a disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).[2] Data obtained by the Task Force for Handling COVID-19 total cases in Indonesia on March 14, 2021, who were confirmed positive for COVID-19 had comorbidities, one of which was diabetes mellitus 33.6%.[3] Data from preliminary studies at One of Hospital Bantul, the total number of cases of inpatients with type 2 DM in 2021 was 667, with a total of 309 type 2 DM patients confirmed with COVID-19 and 358 type 2 DM patients without confirmed COVID-19.

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Based on the Decree of the Minister of Health, because the number of COVID-19 cases is exacerbated by the presence of comorbidities or accompanying diseases that cannot be handled by referral hospitals that have been determined by the government and so that patient services remain optimal, all hospitals that are capable of providing COVID-19 services are encouraged to be involved. Services for COVID-19 patients will be funded by the government. Through the Director General of Health Services, patients who are treated for emerging infections such as COVID-19 infection will have their costs claimed by the Ministry of Health (Kemenkes).[4]

Patients who consider their illness to be serious will try to control the illness they suffer from, for example, by complying with taking medication so that the clinical outcome becomes better than before.[4] Clinically, there is a relationship between the use of health supplements and the success of COVID-19 therapy with comorbid type 2 diabetes mellitus and there are differences in the length of stay (LOS) of diabetes mellitus patients with or without confirmed COVID-19.[52, 53] Patients infected with SARS-CoV-2 with comorbidities DM is very likely to experience significant impairment of glycemic control and ultimately require adjustment of antidiabetic treatment to optimize outcome clinical. Clinical management of DM patients in the COVID-19 era can be very challenging,[5,6] especially in hospitals in patients who must undergo close monitoring of glucose to optimize outcomes clinically.[6,7]

The relationship between COVID-19 and DM is quite complicated and bidirectional. On the one hand, DM is considered a risk factor in the severe course of COVID-19. Several factors frequently present in DM are likely to contribute to this risk, such as older age, proinflammatory and hypercoagulable states, hyperglycemia, and underlying comorbidities (hypertension, cardiovascular disease, chronic kidney disease, and obesity). On the other hand, severe COVID-19 infection and its treatment with steroids may have a specific negative impact on diabetes itself, leading to the worsening of hyperglycemia through increased insulin resistance and decreased β-cell secretory function. Worsening hyperglycemia will ultimately adversely impact the course of COVID-19.[8]

Based on the description above, the author aims to determine whether there are differences or not in the outcome clinical history of diabetes mellitus patients who were confirmed to have COVID-19 and diabetes mellitus patients who were not confirmed to have COVID-19 at the One of Hospital Bantul Regional Hospital through medical records from monitoring blood sugar (GDS) on the 3rd day of treatment.

METHODS

This type of research is observational by design cross-sectional. Secondary data is in the form of medical records to determine whether there is or not the difference in outcome Clinical data from DM patients with or without confirmed COVID-19 at One of Hospital Bantul, Bantul from June to December 2021. This research was carried out afrer obtaining a letter of ethics from the ethics commission of Alma Ata University no. KE//AA//III/10730/EC/2022.

The inclusion criteria in this study are inpatients in the ward (Cempaka, Bakung, Nusa Indah and Rose) and patients ≥ 18 years. Exclusion criteria in this study were that the patient died with in 1 x 24 hours, and the length of treatment was < 3 days, and p Incomplete medical record with GDS data on day 3 of treatment.

Sampling was carried out using the method of simple random sampling with the Lemeshow formula, produce minimum sample size of 36 sample. Data were analyzed using bivariate analysis tests Mann-Whitney Test.

The independent variables in this study are type 2 diabetes mellitus which is confirmed by COVID-19 and type 2

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diabetes mellitus which is not confirmed by COVID-19. The dependent variable in this research is the outcome clinical type 2 diabetes mellitus confirmed by COVID-19 and type 2 diabetes mellitus not confirmed by COVID-19.

Data interpretation is seen from the significance value, namely the hypothesis is accepted if the significant value is <0.05 so it can be interpreted that there are differences between different independent variables, and the hypothesis is rejected if the significance value is >0.05.

RESULTS AND DISCUSSION

Results must be clear and concise. Results should summarize scientific findings by providing very detailed data. It is advisable to point out differences between one's own results or findings and previous publications by other researchers. Like the Methods chapter, the Results and Discussion chapter can also be divided into subchapters. The data presented in the results must be relevant to the objectives and not raw data that still needs to be processed.

Characteristics of research subjects

Of all type 2 diabetes mellitus patients who were hospitalized in Bangsalcempaka, daffodils, nusa beautiful and roses One of Hospital Bantul took 72 type 2 DM patients divided into 2 groups, namely 36 type 2 DM patients with confirmed COVID-19 and 36 type 2 DM patients not confirmed with COVID-19. The characteristics of the research subjects can be seen in the following Table 1.

The gender characteristics of type 2 DM patients confirmed with COVID-19 are mostly women, reaching 52.8%. This is in line with Mustafida's research et al (2022) which states that the majority of COVID-19 patients with diabetes mellitus are female, reaching 64.4%.[9] Apart from that, research conducted by Raran (2022) stated that the majority of COVID-19 patients with diabetes mellitus were female, reaching 56.4%.[10] This happens because the prevalence of diabetes mellitus in Indonesia is more in women with a percentage of 32.7%. Edi Kurnianto's research et al (2021), states that 81.2% of women are more likely to gather than men (71.1%), 87.2% of women are more likely to shake hands than men (75.3%), 77.5% of women are more likely to not maintain a distance of 1 meter than men (68.7%), resulting in a high potential for virus transmission.[11]

Table 1. Characteristics of research subjects

Characteristic	Type 2 DM with COVID 19		Type 2 DM without COVID 19	
	n	%	n	%
Gender				
Man	17	47.2	13	36.1
Women	19	52.8	23	63.9
Age				
18-25 years	0	0	0	0
26-34 years	0	0	1	2.8
35-44 years	5	13.9	2	5.6
45-54 years	5	13.9	9	25.0
55-64 years	15	41.7	16	44.4
65-74 years	10	27.8	7	19.4
≥ 75 years	1	2.8	1	2.8
Total	36	100	36	100

The gender characteristics of type 2 DM patients not confirmed by COVID-19 were mostly women, reaching 63.9%. These results are in line with Muliani's research et al (2021) with the highest gender result being female 34 (75.6%)[12] and research by Ratnasari et al (2020) with the result that women are more than men, reaching 113 (56.5%).[13] This is because the estrogen hormone in women decreases during perimenopause and menopause, causing high cholesterol levels in the body. High cholesterol levels cause an increase in fatty acids, this is the cause of damage to pancreatic β cells and results in diabetes mellitus. Cholesterol itself is one of the causes of increased, diabetes mellitus.[14]

The age of type 2 DM patients confirmed with COVID-19 was mostly 55-64 years, 15 patients (41.7%). These results

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are in line with Mustafida's research et al (2022) which states that the majority of COVID-19 patients with diabetes mellitus are aged 56-65 years (42.2%).[9] Apart from that, Putri also conducted research et al (2021) which states that the majority of COVID-19 patients with diabetes mellitus are aged >50 years (65.5%).[15] This happens because those aged >50 years have higher ACE2 expression and have other conventional factors, for example, decreased organ function, decreased immunity, comorbidities and other causes, thereby increasing the risk of death. In addition, patients aged >50 years were at 15.4 times the risk of death compared with patients aged <50 years. In addition, comorbidities are also associated with a significantly increased risk of death at age >50 years.[15,16]

The age of type 2 DM patients who were not confirmed with COVID-19 was mostly 55-64 years, 16 patients (44.4%). These results are in line with basic health research (2018), which states that the highest prevalence of diabetes mellitus is 55-64 years (6.3%)[17] and Kistianita's research (2018) which states that the majority of patients with type 2 diabetes mellitus at the Kendalkerep Community Health Center, Malang City namely 55-64 years (75%).[18] This happens because at that age, physiologically, body function and secretion decrease or insulin resistance results in a less than optimal ability of the body to control high blood glucose.[19] Increasing age causes insulin resistance which results in unstable blood sugar levels so that one of the incidents of DM is caused by aging factors that cause a degenerative decline in body function.[20,21]

Prevalence of type 2 diabetes mellitus patients at One of Hospital Bantul Regional Hospital for the period June-December 2021

The data results obtained show the prevalence of type 2 diabetes mellitus There were 185 patients (50.3%) confirmed with COVID-19. It is known that out of 185 type 2 DM patients, 96 patients had complications, 2 patients died within 1 x 24 hours and 11 patients had treatment duration < 3 days. These results are in line with Badawi's research et alregarding A systematic analysis of 637 MERS-CoV cases showed that approximately 50% of patients had diabetes.[22] This is also in line with Bhatraju's research et al which stated that the prevalence of diabetes in COVI-19 was 58%.[23] Chen's research results et al (2020) said that 14-32% of patients with diabetes are more susceptible to critical forms of the disease.[24] The prevalence of diabetes in COVID-19 was found to be quite variable, in two separate studies conducted in northern Sudan the results were 18.7% and 19.1%.[25,26]

Table 2. Prevalence of diabetes mellitus patients at One of Hospital Bantul for the period June-December 2021

DM type 2	n	%
DM type II confirmed with COVID-19	185	50.3
DM type II is not confirmed with COVID-19	183	49.7
Total	368	100

The data obtained shows the prevalence of type 2 diabetes mellitus There were 183 patients (49.7%) not confirmed with COVID-19. It is known that of the 183 type 2 DM patients, 130 patients had complications, 3 patients died with in 1 x 24 hours and 4 patients had treatment duration <3 days. The prevalence of diabetes varies from 1.28% in West Java province to 10.5% globally.[27,28] The differences between these studies may be related to the number of included studies, sample size, and characteristics of the patients included.[24]

WHO states that around 150 million people in the world suffer from diabetes mellitus.[29] WHO also states that the prevalence of diabetes is increasing in low and middle-income countries,[30] this explains why the prevalence of diabetes in One of Hospital Bantul is the fourth highest after COVID-19, pneumonia, and single ton. The prevalence of diabetes in Indonesia is the seventh highest in the

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world after China, India, the United States, Brazil, Russia and Mexico.[31]

Outcome clinical type 2 DM patients confirmed with COVID-19 and type 2 DM patients not confirmed with COVID-19

Table 3. Differences in clinical outcomes of type 2 DM patients with confirmed COVID-19 and type 2 DM patients not confirmed with COVID-19 on day 3 of treatment (n=36)

Clinical outcomes	DM type II with COVID -19		DM type II without COVID -19		p-value
	n	%	n	%	
Controlled GDS (<200 mg/dL)	14	38.9	20	55.6	0.046
Not controlled GDS (≥200 mg/dL)	22	61.1	16	44.4	

Outcome clinical type 2 DM patients confirmed with COVID-19

Outcome clinical trials in this study were seen on day 3 of treatment because the aim of this study was to see comparisons, so as to see Outcome clinical type 2 DM patients confirmed with COVID-19 and Outcome clinical type 2 DM patients who were not confirmed to have COVID-19 seen on the same day. Apart from that, the reason it was seen on the 3rd day of treatment was because when a preliminary study was carried out the average length of treatment for type 2 DM patients at the One of Hospital Bantul Regional Hospital was 3 days.

This research showed that 22 type 2 DM patients had confirmed COVID-19 outcome uncontrolled clinical GDS (≥200 mg/dL) (61.1%). This research looks at outcome clinical data from GDS values alone due to limited data on HbA1c, GDP and G2PP. This research is in line with Endarti's research et al (2020) who stated that in their research they saw outcome clinically from the GDS value alone.[13]

These results are in line with Widiastuti's research et al (2021) showing that the majority of respondents had abnormal GDS examination results with 43 people (82.7%).[32] This study is also in line with research by Zhu (2020) from Hubei Province in China, including 7,337 type 2 DM inpatients with confirmed COVID-19 with poor outcomes and higher mortality rates compared with COVID-19 without DM.[33] In line with research by Yuanyuan (2021), COVID-19 patients with type 2 DM have higher blood glucose levels than those without type 2 DM, leading to severe clinical outcomes.[34] This is because COVID-19 infection will exacerbate stress in DM patients by releasing glucocorticoids and catecholamines into the circulation, thereby worsening glycemic control and increasing the formation of glycation end products in many organs and worsening the prognosis.[35]

It is also known that some patients' GDS at the time of admission is higher than on the first day of admission. This can occur due to several factors such as increasing the amount of food consumed, increasing stress and emotional factors, increasing body weight and age, as well as the impact of drug treatment, for example, steroids.[36]

SARS-CoV2 may affect glycemic control. It is known that any acute illness or inflammatory condition can increase insulin resistance and blood glucose levels.[37] Of note, among 1,122 hospitalized patients with COVID-19 at 88 US hospitals, approximately 40% had uncontrolled DM or hyperglycemia on admission.[38] It was later discovered that binding of SARS-CoV2 to its receptor, angiotensin-converting enzyme 2 (ACE2), in the endocrine part of the pancreas, can directly damage pancreatic islets and reduce insulin secretion and cause DM.[39,40]

Severe COVID-19 infection and its treatment with steroids, may have a specific negative impact on diabetes itself, leading to worsening of hyperglycemia through increased insulin resistance and decreased β-cell secretory function.

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Worsening hyperglycemia will ultimately adversely impact the course of COVID-19.[8]

In contrast, high glucose levels contribute to the risk of acute respiratory distress syndrome in COVID-19 patients[41] and hyperglycemia was identified as a poor prognostic marker for pneumonia outcome[42] The role of hyperglycemia in the development and prognosis of COVID-19 remains speculative, potential mechanisms that increase susceptibility to COVID-19 in patients with DM include higher affinity cellular binding for more efficient viral entry, inhibition of viral clearance, impaired T cell function.[43]

Outcome clinically, type 2 DM patients were not confirmed to have COVID-19

A total of 20 type 2 DM patients were not confirmed to have COVID-19 in this study outcome controlled clinical GDS (<200 mg/dL) (55.6%). These results are in line with research by Sepamarin et al (2021) which was carried out at the Kasih II health center and research by Aprilia et al (2021) at Gamping 1 Community Health Center with the results outcome More clinic patients with type 2 DM are controlled (GDS <200 mg/dL) compared to those who are not controlled (GDS ≥200 mg/dL).[44,45]

The purpose of blood glucose examination is to determine whether the therapeutic goal has been achieved and can be used as an indicator to adjust the drug dose if the therapeutic goal has not been achieved.[46] Parameter outcome The clinical method used in this research is GDS, which is a measurement of blood glucose levels that can be measured at any time, regardless of the last time the patient ate.[47]

Regular blood sugar checks are useful for preventing increases in blood sugar and preventing complications.[48] According to Kurniawati, quoted by Lestari et al (2013), the older a person is, the greater the risk of increased glucose levels and impaired glucose tolerance. This is caused by disruption of all body organ functions, including pancreatic cells which are responsible for producing insulin. Pancreatic cells can be degraded, resulting in the production of too little insulin hormone resulting in high blood sugar.[49] Soegiarto's (2013) research quoted by Rahmawati (2015) states that an increase in blood sugar is not only due to schedule irregularities but there are other factors such as stress, diet and lack of activity.[50]

Difference Outcome Clinical Type 2 DM Patients with Type 2 DM Patients Confirmed with COVID-19 on the 3rd Day of Treatment

Based on the Mann-Whitney Test There was a significant difference in the GDS value on the 3rd day of treatment, p=0.046 for type 2 DM with confirmed COVID-19 and type 2 DM with no confirmed COVID-19. This shows that diabetes mellitus patients who are confirmed to have COVID-19 have outcome different clinical conditions from diabetes mellitus that is not confirmed by COVID-19. Type 2 DM patient confirmed with COVID-19 show Outcome GDS clinical conditions are worse when compared with type 2 DM patients not confirmed by COVID-19.

This research is in line with You's research et al (2020), COVID-19-positive patients with type 2 DM show different clinical outcomes from COVID-19-positive patients without type 2 DM, whereas COVID-19-positive patients with type 2 DM show worse clinical outcomes such as the risk of ICU admission. and higher in-hospital mortality than those without type 2 DM.[51] This research is also in line with research by Bode (2020) which states that hypoglycemic glucose concentrations (blood glucose <70 mg/dL) occur more often in patients with diabetes and/or hyperglycemia, occurring on 137 of 3885 patient days (3.5%) compared with 39 of 3793 days in patients without diabetes or hyperglycemia. (1.0%, P<0.001). Likewise, severe hypoglycemia (blood glucose <40 mg/dL) was significantly more common in the diabetes and/or hyperglycemia group, occurring in 25 patient days (0.6%) compared with 3 patient days in those

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without diabetes or no hyperglycemia. controlled (0.1%, P < .001).

Difference outcome Clinical GDS occurs due to an acute illness, in this case, COVID-19, which can increase insulin resistance and worsen glucose levels.[37] Besides that, steroid treatment will worsen hyperglycemia by increasing insulin resistance and decreasing β-cell secretory function.[8] With differences outcomes clinical GDS type 2 DM confirmed with COVID-19 and type 2 DM not confirmed with COVID-19, it is necessary to carry out optimal glycemic control not limited to GDS alone but with other blood glucose parameters such as HbA1c, GDP and G2PP to see whether the patient's glucose level controlled or not. So it can prevent increased blood sugar and complications.

CONCLUSION

Test results Mann-Whitney Test significant differences were found outcome clinical p=0.046 type 2 DM confirmed with COVID-19 and type 2 DM not confirmed with COVID-19. DM patients who are confirmed to have COVID-19 have outcomes clinically different from DM which is not confirmed by COVID-19.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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