**Journal of Medical and Health Studies**
ISSN: 2710-1452
DOI: 10.32996/jmhs
Journal Homepage: www.al-kindipublisher.com/index.php/jmhs

JMHS
AL-KINDI CENTER FOR RESEARCH AND DEVELOPMENT

**| RESEARCH ARTICLE**

# Comparison of Kendali Glycemia during and Post-Hospitalization in Covid-19 Patients with Diabetes Mellitus at AR Bunda Prabumulih Hospital

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**| ABSTRACT**

The study compared therapeutic modalities and changes in hypoglycemic agents with glycemia control seen from blood sugar levels and HbA1C in COVID-19 and Diabetes Mellitus patients. This study was followed at three months and six months post-COVID-19. This study is a prospective cohort study with a 3-point cross-sectional crossectional approach. Data is also taken from medical record data, followed by post-covid-19 months three and 6. In this study, it can be concluded that blood glucose levels during three months and six months after COVID-19 are still difficult to control, even though there has been a change in the therapeutic modality from OAD to insulin. There is a decrease in the average HbA1c levels three months after COVID-19 and six months after COVID-19, statistically means p.

**| KEYWORDS**

Glycemia, Covid-19, Diabetes Mellitus

**| ARTICLE INFORMATION**

**ACCEPTED:** 28 February 2023 **PUBLISHED:** 11 March 2023 **DOI:** 10.32996/jmhs.2023.4.2.7

## 1. Introduction

Since December 2019, acute coronavirus 2 (SARS-CoV-2) infection in the respiratory system is still a worldwide health problem. Had mellitus associated with an increased risk and severity of coronavirus disease 2019 (COVID-19)? In interaction with various other risk factors, high blood sugar levels can lower the immune system and increase the replication of SARS-CoV-2. Occupational stress and more fantastic release of pro-inflammatory cytokines in diabetic individuals than in healthy people can worsen SARS CoV-2 infection in diabetics. In addition, COVID-19 also causes hyperglycemia in individuals with diabetes, which may be associated with insulin resistance and pancreatic β cell dysfunction during SARS-CoV-2 infection. Research data since the beginning of the COVID-19 outbreak reported that approximately 25.1% of COVID-19 sufferers had one or more underlying comorbid diseases, such as hypertension (16.9%) and diabetes (8.2%), heart disease (7.1%), asthma and COPD (5.3%). Data from RSMH palembang 2021, covid-19 sufferers with comorbid diabetes are around 13-15%. In addition, diabetes mellitus is the second comorbid disease in the void-19 pandemic that has died.

The study aimed to compare therapeutic modalities and changes in hypoglycemic agents with glycemia control seen from blood sugar levels and HbA1C in COVID-19 and Diabetes Mellitus patients. The study was followed at three months and six months post-COVID-19.

## 2. Research Methods and Design

This study is a prospective *cohort* study with a *3-point cross-sectional crossectional* approach. Data is also taken from *medical record* data, followed by post-covid-19 months 3 and 6. This research was conducted from January to December 2021 at the AR Bunda

Prabumulih hospital. Data and research results are displayed in tables, graphs, and statistical analysis of univariate and bivariate with *chi-square* and *Wilcoxon*

**3. Results**

This study followed 72 COVID-19 patients with DM, 30 men (41.7%) and 42 women (53.3%), with an average age of 57.15±10.02 years. Patients with COVID-19 are moderately symptomatic with comorbid diabetes mellitus and are declared a negative PCR test upon returning home from the hospital.

**Table 1. Demographic data and clinical characteristics of the study population**

| Demographic and Clinical Data | Mean, SD, N | Percentage (%) |
|---|---|---|
| Age (years) | 57,15±10,02 | |
| Gender | | |
| Man | 30 | 41,7 |
| Woman | 40 | 58,3 |
| IMT (kg/m$^2$) | 29±1,40 | |
| LOS/*length of stay* (hari) | 9,88±2,38 | |
| Hemoglobin (gr/dl) | 12,54±1,80 | |
| Leukocytes (/mm$^3$ ) | 7812±4824 | |
| CRP (gr/L) | 61,58±36,29 | |
| Total cholesterol (mg/dl) | 217,65±49,31 | |
| Triglycerides (mg/dl) | 217,65±49,31 | |
| HDL (mg/dl) | 47,81±6,93 | |
| LDL (mg/dl) | 174,93±35,67 | |
| Urea (mg/dl) | 33,55±16,99 | |
| Creatinin (mg/dl) | 0,85±0,30 | |

Table 1 shows most obese category patients with BMI 29±1.40 kg/m $^2$, with hemoglobin 29±1.40 gr/dl, leukocytes 812±4824/mm$^3$, CRP 61.58±36.29 gr/L, total sterol cabbage 217.65±49.31 mg/dl, triglycerides 217.65±49.31 mg/dl, HDL 47.81±6.93 mg/dl, LDL 174.93±35.67 mg/dl, serum 33.55±16.99 mg/dl, creatinine 0.85±0.30 mg/dl. These data show metabolic decompensation in COVID-19 patients with diabetes mellitus: obesity, impaired lipid profile, and increased CRP markers of acute inflammation.

At the time of initial hospital admission, patients with COVID-19 were identified whether oral hypoglycemic agents or injections were used. The anamnesis showed most sufferers with a history of diabetes mellitus: 60 people (83.3%) and 12 people (16.7%) with no previous history of diabetes mellitus, as in table 2.

**Table 2. The relationship of sugar levels at the time of hospital admission with the type of therapy**

| Initial Therapy during MRS (T0) | GDS <200 mg/dl | GD ≥ 200 mg/dl | Total |
|---|---|---|---|
| Oral antidiabetik (OAD) | 10 (13,9%) | 33 (45,8%) | 43 (59,7%) |
| Combination of OAD and insulin | 2 (2,8%) | 7 (9,7%) | 9 (12,5%) |
| Insulin basal bolus | 2 (2,8%) | 6 (8,3%) | 8 (11,1%) |
| No antidiabetic drugs | 2 (2,8%) | 10 (13,9%) | 12 (16,7%) |
| **Total** | 16 (22,2%) | 56 (77,8%) | 72 (100%) |

In table 2, it is seen at the time of hospital admission: 56 people (77.8%) of sugar levels when (GDS) were above average, and most of the 43 people (59.75%) with oral antidiabetic therapy (OAD). After statistical testing, it was found that **p<0.962** had no meaningful relationship between the type or modality of therapy and the current blood sugar profile.

**Table 3. The relationship of sugar levels at the time of discharge with the type of therapy**

| Types of Therapy while in the hospital | GDS <200 mg/dl | GDS ≥ 200 mg/dl | Total |
|---|---|---|---|
| Oral antidiabetik (OAD) | 5 (6,9%) | 0 | 5 (6,9%) |
| Combination of OAD and insulin | 10 (13,9%) | 1 (1,4%) | 11 (15,3%) |
| Insulin basal-bolus | 41 (56,9%) | 15 (20,8%) | 56 (77,8%) |
| **Total** | 56 (77,8%) | 16 (22,2%) | 72 (100%) |

In table 3, it can be seen that when returning home from treatment from RS, 56 people (77.8%) ka dar sugar when (GDS) was expected, and 16 people (22.2%) GDS was still above 200 mg/dl, here it was seen that the difficulty of glycemia control in COVID-19 passion with diabetes mellitus although most of the 56 people (77.8%) with basal-bolus insulin injection. After the statistical test was conducted, p**<0.106,** there was no meaningful relationship between the type or modality of therapy and the current blood sugar profile. These data show the change in hypoglycemia drug agents from OAD to basal-bolus insulin or a combination of OAD dan insulin.

**Table 4. Relationship of blood sugar levels three months post-covid with the type of therapy**

| Types of therapy while in the hospital | GDS <200 mg/dl | GDS ≥ 200 mg/dl | Total |
|---|---|---|---|
| Oral antidiabetik (OAD) | 7 (9,7%) | 6 (8,3%) | 13 (18,1%) |
| Combination of OAD and insulin | 10 (13,9%) | 8 (11,1%) | 18 (25,0%) |
| Insulin basal-bolus | 17 (23,6%) | 24 (33,3%) | 41 (56,9%) |
| **Total** | 34 (47,2%) | 38 (52,8%) | 72 (100%) |

In table 4, it is seen that at the time of control three months post-COVID-19, there were 34 (people) with 47.28% sugar levels when standard, and most of the 17 people (23.68%) with basal-bolus insulin injection, but there were 38 people (52.8%) when sugar levels (GDS) were still more than 200 mg/dl. This shows the difficulty of glycemia control in post-COVID-19 patients. After statistical testing, it was found that **p<0.528** had no meaningful relationship between the type or modality of therapy and the current blood sugar profile.

**Table 5. Relationship of blood sugar levels six months post-covid**

| Types of therapy while in the hospital | GDS <200 mg/dl | GDS ≥ 200 mg/dl | Total |
|---|---|---|---|
| Oral antidiabetik (OAD) | 9 (12,5%) | 4 (5,6%) | 13 (18,1%) |
| Combination of OAD and insulin | 13 (18,1%) | 5 (6,9%) | 18 (25,0%) |
| Insulin basal-bolus | 26 (36,1%) | 15 (20,8%) | 41 (56,9%) |
| **Total** | 48 (66,7%) | 24 (33,3%) | 72 (100%) |

Table 5 shows that during the 6-month post-COVID-19 control, there were 48 people (66.7%) with sugar levels when they were normal, and 24 people (33.3%) with sugar levels were still abnormal—most 41 people (56.9%) with use of basal-bolus insulin injection. After statistical testing, it was found that p<0.528 had no meaningful relationship between the kind or the modality of therapy and the current blood sugar profile.

**Table 6. The relationship between the type of therapy and the profile of HbA1C at the time of hospital admission**

| Initial Therapy during MRS | HbA1C <7.5% | HbA1C ≥ 7,5 % | Total |
|---|---|---|---|
| Oral antidiabetik (OAD) | 2 (2,8%) | 41 (56,9%) | 43 (59,7%) |
| Combination of OAD and insulin | 0 | 9 (12,5%) | 9 (12,5%) |
| Insulin basal bolus | 0 | 8 (11,1%) | 8 (11,1%) |
| No antidiabetic drugs | 0 | 12 (16,7%) | 12 (16,7%) |
| **Total** | 2 (2,8%) | 70 (97,2%) | 72 (100%) |

In table 6, it can be seen that at the time of entering the hospital profile HbA1C (H0), most of them were above 7.5%, as many as 70 people (**97.2**%), and most of the 43 people (59.7%) with oral antidiabetics (OAD). After statistical testing, it was found that **p<0.552** had no meaningful relationship between the type or modality of therapy and the HbA1C profile.

**Table 7 Development of mean sugar levels during patients T0, T1, T2, T3**

| GDS | Mean | Median | SD |
|---|---|---|---|
| GDS on entry R(T0) (mg/dl) | 265,72 | 278,00 | 90,85 |
| GDS home (T1) (mg/dl) | 165,84 | 149,50 | 66,36 |
| GDS 3 months post covid (T2) (mg/dl) | 202,22 | 200,00 | 61,68 |
| GDS 6 months post covid (T3) (mg/dl) | 167,04 | 150,50 | 59,29 |

In table 7, the average GDS at admission RS (T0): 265.72 mg/dl was obtained and decreased to the standard limit when returning from RS (T1): 165.84 mg/dl. At three months post-COVID-19 (T2), there was an average increase to **202.22** mg/dl, and at the

evaluation of 6 months post-COVID-19 (T3) to 167.04 **mg/dl**. After statistical tests, it was found that **p<0.021,** there was a meaningful relationship between changes in sugar levels during T0, T1, T2, and T3.

**Table 8. Relationship of type of therapy and HbA1C 3 months post covid**

| Types of treatment while in the hospital | HbA1C <7.5% | HbA1C ≥ 7,5 mg/dl | Total |
|---|---|---|---|
| Oral antidiabetik (OAD) | 2 (2,8%) | 11 (15,3%) | 13 (18,1%) |
| Combination of OAD and insulin | 0 | 18 (25,0%) | 18 (25,0%) |
| Insulin basal-bolus | 1 (1,4%) | 40 (55,6%) | 41 (56,9%) |
| **Total** | 3 (4,2%) | 69 (95,8%) | 72 (100%) |

Table 8 shows that during the follow-up three months after COVID-19, the HbA1C profile was mainly above 7.5%, as many as 69 people (95.8%), although most of the 41 people (56.9%) were injected with basal-bolus insulin. After statistical testing, it was found that **p<0.112** had no meaningful relationship between the type or modality of therapy and the HbA1C profile. These data showed that glycemia control in COVID-19 patients with diabetes mellitus after three months post-COVID-19 only slightly reached HbA1C <7.5%: 3 people (4.2%).

**Table 9. Relationship of type of therapy and Hb1AC 6 months post covid**

| Types of treatment while in the hospital | HbA1C <7.5% | HbA1C ≥ 7,5 mg/dl | Total |
|---|---|---|---|
| Oral antidiabetik (OAD) | 2 (2,8%) | 11 (15,3%) | 13 (18,1%) |
| Combination of OAD and insulin | 1 (1,4%) | 17 (23,6%) | 18 (25,0%) |
| Insulin basal-bolus | 1 (1,4%) | 40 (55,6%) | 41 (56,9%) |
| **Total** | 4 (5,6%) | 68 (94,4%) | 72 (100%) |

Table 9 shows that during *the follow-up* six months after COVID-19, the HbA1C profile was mainly above 7.5%, as many as **68 people (94.4**%), although most of the 41 people (56.9%) were injected with basal-bolus insulin. After statistical testing, it was found that **p<0.272** had no meaningful relationship between the type or modality of therapy and the HbA1C profile.

**Table 10. The average development of HbA1C patients pis present when H1,H2,H3**

| Up to HbA1C | Median | Min-Max |
|---|---|---|
| HbA1C upon admission RS (H1) (%) | 10,40 | (6,0-15,0) |
| HbA1C 3 post-covid bualn (H2) (%) | 10,20 | (5,8-14,8) |
| HbA1C 6 months post covid (H3) (%) | 8,00 | (6,0-12,0) |

Table 10 shows the average HbA1C at hospital admission (H1): 10.40% (6.0-15.0), HbA1C at three months post-COVID-19 *follow-up* (H2): 10.20% (5.8-14.8), HbA1C at six months post-COVID-19 evaluation (H3): 8.00% (6.0-12.0 ). After statistical tests of changes in the index of HbA1C from H1 to H2 with p<0.042, H2 to H3 with n p<0.0001, and H1 to H2 to H3 with **p<0.0001** are statistically meaningful, even though the target is still a lot of HbA1C has not been achieved**.**

**4. Discussion**

Diabetes mellitus and COVID-19 are both diseases that are burdensome to each other and can also be co-incidences. Diabetes can increase the inflammatory process in COVID-19, prolong the treatment day, and aggravate complications. COVID-19 can complicate the control of glycemia, exacerbating macro and microvascular complications. In this study, of 792 patients suspected of COVID-19, there were 1 19 people (15.02%) with diabetes mellitus and 254 people (32.07%) with hypertension. Singh et al. 2020, there is an approximately 5.3-58.0% prevalence of DM with COVID-19, with a critical or severe clinical picture or manifestation of 14-23%. Abdi et al. showed a majority of DM with COVID-19 of about 14.5% and were prone to severe clinical and mortality. Seventy-two confirmed covid-19 patients with DM followed the study, 30 men (41.7%) and 42 women (53.3%), averaging 57.15±10.02 years. Other studies have shown DM to be responsible for various complications in COVID-19 patients, such as hypertension, hyperlipidemia, obesity, cardiovascular disease, and arrhythmias. Diabetic patients with comorbidities are particularly susceptible to COVID-19. The severity and mortality from COVID-19 are very high in people with diabetes and other comorbidities. The study was taken on moderately confirmed COVID-19 with comorbid diabetes Mellitus—the duration of treatment at the hospital averages 9.88±2.38 days.

At the time of hospital admission, patients with COVID-19 were identified whether oral hypoglycemic agents or injections were used. The anamnesis showed most sufferers with a history of diabetes mellitus: 60 people (83.3%) and 12 people (16.7%) without previous risk of diabetes mellitus. Sing AK et al. show that COVID-19 and Diabetes Mellitus or CoviDIAB patients can be categorized into four groups: 1. stress hyperglycemia, 2. new-onset diabetes, 3. *associated* hyperglycemia with SAR-CoV-2, 4. *in hospital hyperglycemiA* (glucocorticoid induce hyperglycemia). In this study, blood sugar levels (GDS) were present when entering the hospital: 56 people (77.8%) had sugar levels while (GDS) were above average, and most of the 43 people (59.75%) with oral antidiabetic therapy (OAD). After conducting statistical tests, it was found that **p<0.962** had no meaningful relationship between the type or modality of therapy and the current blood sugar profile.

SARS-CoV-2 may induce cytokine storms, an excessive immune response with the production of pro-inflammatory cytokines of the ic system, which may play a role in facilitating insulin resistance, damage, and death or apoptosis of pancreatic beta cells. This study averaged GDS at hospital admission (T0): 265.72 mg/dl and decreased to the standard limit when returning from the hospital (T1): 165.58 mg/dl, control three months post-COVID-19. There was an increase in average to **202.22** mg/dl and in the evaluation six months post-covid to 167.04 mg/dl. After statistical tests, it was found that **p<0.021,** there was a meaningful relationship between changes in sugar levels during T0, T1, T2, and T3. Wang et al. 2020 showed increased blood glucose levels in patients post-covid-19 until the 28th day of post-hospital treatment. Lie et al. 2021 uncontrolled post covid glucose levels are likely to increase pancreatic s el beta damage, peripheral insulin resistance, and gluconeogenesis in hepar.

To see the control of glycemia in the last three months, it is necessary to check HbA1C levels. In this study, the average HbA1C when entering the hospital (H1): was 10.40% (6.0-15.0), with 70 people (97.2%) still ≥7.5%, HbA1C when *following up three* months after COVID-19 (H2): 10.20% (5.8-14.8) with 69 people (95.8%) still above ≥7.5%, HbA1C during evaluation six months after covid-19 (H3): 8.00% (6.0-12.0), 94 people (94.4%) still above ≥7.5%. After statistical testing, the change in the index of HbA1C from H1 to H2 with p<0.042, H2 to H3 with p<0.0001, and H1 to H2 to H3 with **p<0.0001** is statistically meaningful, even though the average target has not been achieved HbA1C. This data shows a decrease in HbA1C, but many people have not reached the target of <7.5%. Montefusco L et al. 2021, Glycemia abnormalities in COVID-19 patients can be detected for at least up to 2 months in patients who recover from COVID-19 in patients who were previously normoglycemia (non-diabetic). The study found that 46% of the 551 patients were hyperglycemia.

Previous studies revealed that diabetic patients with COVID-19 were at high risk of cardiovascular disease (20.9%), hypertension (56.9%), and cerebrovascular disease (7.8%) compared to non-diabetics. Long-term diabetics are at risk for various comorbidities such as nervous system diseases, chronic diseases, and kidney disease. Recent studies have shown that SARS-CoV-2 damages the kidneys through the ACE-2 pathway. It was found that SARS-CoV-2 can cause cell damage directly, and insulin resistance accompanied by hypokalemia, cytokine, and fetuin-A levels may also worsen in diabetic patients with COVID-19. Cardiovascular disease, the collective comorbidity of endocrine diseases consisting of DM, is an essential contributor to COVID-19 morbidity

**5. Conclusion**

Infection with SARS-CoV-2 with diabetes mellitus will jointly lead to high susceptibility, and the severity of the disease will increase. The pathogenic link between DM and COVID-19 includes altered glucose homeostasis, increased cytokine release leading to cytokine storms, and increased oxidative stress. This study can be concluded:

1. Blood glucose levels(GDS) 3 months and six months post-COVID-19 are still difficult to control, even though there has been a change in the therapeutic modality from OAD to insulin.
2. There is a decrease in the average HbA1c levels three months after COVID-19 and six months after COVID-19, and statistically, it is nap<0.0001 even though the HbA1C target has not been achieved.

**Funding:** This research received no external funding.

**Conflicts of Interest:** The authors declare no conflict of interest.

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## References

[1] Gerganova A, Assyov Y, Kamenov Z (2022). Stress Hyperglycemia, diabetes mellitus, and COVID-19 infection: Risk factor, Clinical outcomes, and post-discharge implications; *frontiers in clinical diabetes and healthcare 3*: 1-13

[2] Landstar CP, and de Koning EJ. (2021). COVID-19 and diabetes: understanding the interrelationship and risk for a severe course; frontiers in endocrinology; 12: 1-18

[3] Li G, Chen Z, Zhan L and Li H (2021). Diabetes mellitus and COVID-19: associations and possible mechanisms; *Hindawi International journal of endocrinology*: 1-10

[4] Lim S, Bae JH, Kwon HS (2021). COVID-19 and diabetes mellitus: from pathophysiology to clinical management; natural reviews endocrinology; 17: 11-30

[5] Montefusco L, Nasr MB, D'addio F (2021). acute and long-term disruption of hypometabolic control after SARS CoV-2 infection; Nature metabolism 3: 774-85

[6] Nasar M, Daoud A and Nso N (2021). Diabetes and COVID-19: review article; diabetes & metabolic syndrome: *clinical research &reviews;* 15: 1-8

[7] Reshad RA, Riana SH, Chowdhury MA (2021). l: Diabetes in COVID-19 patients: challenges and possible management strategies; *The Egyptian journal of broncho logy*; 1-1