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Case Report: A Confirmed COVID-19 in Newly Diagnosed Diabetes Mellitus Patient

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Abstract: COVID-19 is caused by a novel coronavirus known as SARS-CoV-2, a single chain RNA virus with a particle size of 120-160 nm. Covid-19 can affect almost all age groups, despite, the elderly and people who have records of chronic disease (co-morbid) have the risk to be affected more often and with worse complications from this disease. Diabetes mellitus (DM) is one of the risk factors for enhancing the severity of COVID-19 infection. A 26 years old man, was referred to the hospital with symptoms of shortness of breath, fever, and cough. The patient has no history of comorbidities, but his father has newly type-2 diabetes mellitus (T2DM). The patient was examined, with ad random blood sugar of 220 mg/dL and a chest radiograph suggesting bronchopneumonia. The patient was then examined for fasting and postprandial glucose, HbA1c, and diagnosed with DM, the patient's throat swab showed a positive COVID-19 result. Patients were then treated with antiviral, antibiotic, regulated insulin, and his blood sugar was monitored. The patient's blood sugar is stable and the patient discharge after 34 days of hospitalization.

Keyword: SARS-CoV-2; COVID-19; Diabetes Mellitus; Blood Glucose; Insulin

Abstrak: *COVID-19 merupakan penyakit yang disebabkan oleh infeksi coronavirus baru yang dikenal dengan SARS-CoV-2, virus RNA rantai tunggal dengan ukuran partikel 120-160 nm. Covid-19 dapat menyerang hampir seluruh kalangan usia, namun demikian, kelompok usia lanjut dan orang yang mempunyai riwayat penyakit kronis (ko-morbid) memiliki risiko untuk terkena lebih sering dan dengan komplikasi yang lebih buruk dari penyakit ini. Diabetes Melitus (DM) merupakan salah satu faktor risiko meningkatnya keparahan infeksi COVID-19. Seorang pria, usia 26 tahun, dirujuk ke rumah sakit dengan gejala sesak nafas, demam, dan batuk. Pasien tidak memiliki riwayat penyakit komorbid, namun ayah pasien mengidap diabetes mellitus tipe 2 (DMT2 baru). Pasien dilakukan pemeriksaan, dengan hasil gula darah sewaktu 220mg/dL dan hasil foto thoraks kesan pneumonia. Pasien selanjutnya dilakukan pemeriksaan KGDn/2jpp, HbA1c dan di diagnosis dengan DM, hasil swab tenggorokan pasien menunjukkan hasil positif COVID-19. Selanjunya pasien diterapi dengan antiviral, antibiotik, pemberian insulin, dan dilakukan pemantauan gula darah. Gula darah pasien stabil dan pasien pulang setelah menjalani rawatan selama 34 hari.*

Kata Kunci: *SARS-CoV-2*; *COVID-19*; *Diabetes Mellitus*; *Gula Darah*; *Insulin*

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1 Introduction

Coronavirus disease 2019 (COVID-2019) is caused by a novel coronavirus known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), a single chain RNA virus with a particle size of 120-160nm [1, 2]. Covid-19 can affect almost all age groups, however, the elderly and people who have a history of chronic disease (co-morbid) have the risk to be affected more often and with worse complications from this disease [3]. Diabetes Mellitus (DM) is one of the risk factors for increasing the severity of COVID-19 infection. Diabetics are older (> 60 years), blood sugar levels are not controlled, and the presence of diabetes complications is associated with a poor COVID-19 prognosis [4]. So far, there has been no officially approved drug or anti-SARS-CoV-2 vaccine for COVID-19 treatment, in several ongoing clinical trials. Nonetheless, specific aspects of diabetes management with COVID-19 includes glycemic control and blood sugar monitoring [5]. This case presentation describes a successful experience with blood glucose management in a confirmed COVID-19 patient with diagnosed newly type 2 diabetes mellitus (T2DM).

2 Case Illustration

A 26 years old man, was referred to the H. Adam Malik central public hospital on May 19th, 2020, with chief complaints of shortness of breath. This was experienced by patient approximately 1 day before admission to the hospital, shortness of breath experienced continuously, tightness is not related to activity nor weather. Patient admitted that while breathing the patient felt heavy and felt unsatisfied after breathing. Complaints of tightness accompanied by a dry cough experienced three days before admission to the hospital. The cough was experienced indefinitely and is not affected by activity without phlegm or blood. Fever was also experienced by patients approximately 4 days before being admitted to the hospital, fever is up and down, fever down with fever-lowering drugs. The patient complained of swallowing pain and nasal congestion, a history of allergies was not found. A history of traveling out of town was not found, a history of exposure to COVID-19 patients was not found. Nausea was not found; vomiting was not found. Urination is found within normal limits; defecation is found within normal limits. History of the same disease, diabetes mellitus and hypertension are absent, a history of pulmonary tuberculosis was denied. The father of the patient has a history of type-2 diabetes mellitus.

From the examination, patient with body weight 78 kg and height 165 cm with BMI 28.65 Kg/m^2 were obese. The pulse rate was 102 times/min, blood pressure of 120/70mmHg, a respiratory rate of 26 breaths/min, a temperature of 36.8^oC, and arterial oxygen saturation of 98% with the oxygen of 10L/min via a non-rebreathing mask. Physical examination of the lung found bronchial breath sounds with crackles in the middle field of the right and left lungs, another physical examination within normal limits. From a complete blood count, patients with Hb 14.5g/dL, leukocytes 4,620/µL, platelets of 139,200/µL, neutrophils 65%, and lymphocytes 26%. From the blood gas

analysis, patient with pH/pCO_2/pO_2/HCO_3/TCO_2/BE/SO_2: 7,460/22/164,0/15,6/16,3/-6,4/99,5. The patient's ad-random blood glucose was 220mg/dL with a non-reactive rapid test of COVID-19. From electrocardiogram, it was found sinus tachycardia (Fig. 1). From the chest radiograph, there were infiltrates in both lungs, mainly in the paracardial area with a suggestion of bronchopneumonia and aortic elongation (Fig. 2).

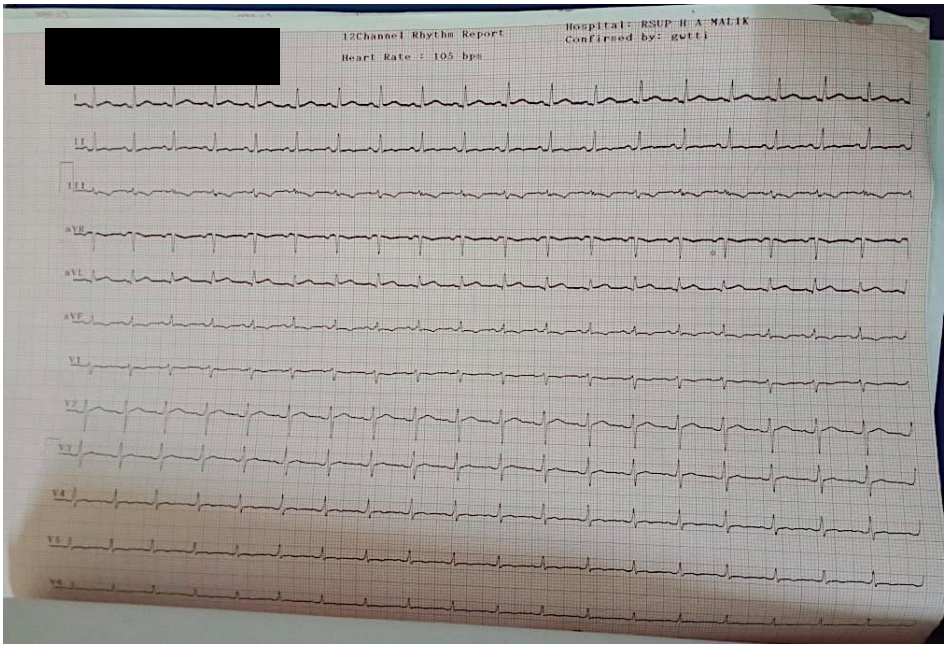

Figure 1. Patient's ECG on May, 19th, 2020

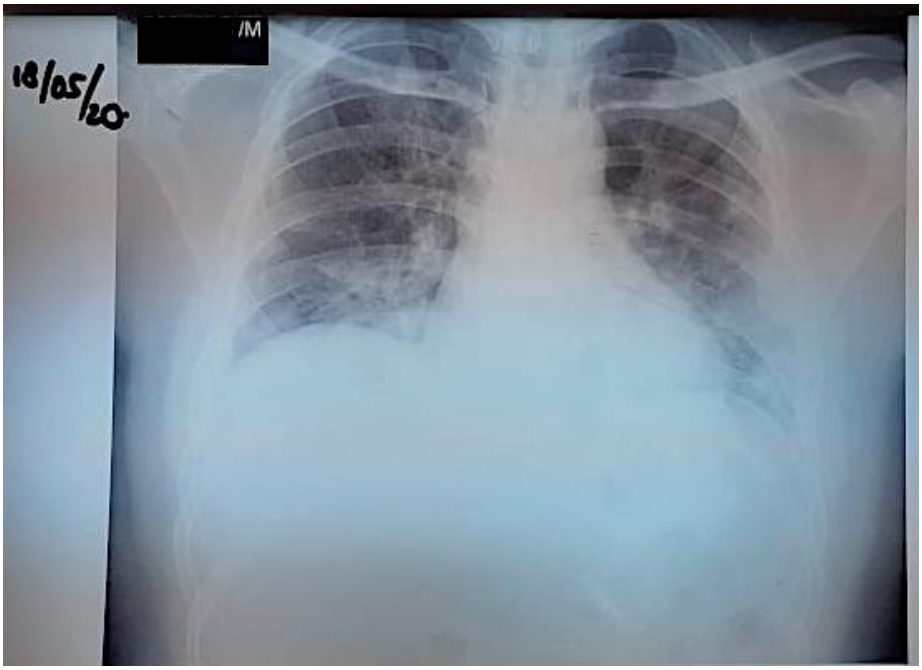

Figure 2. Patient's chest x-ray on May, 18th, 2020

Patient was diagnosed with a moderate degree suggestion of COVID-19 with stress hyper glycemia dd/ T2DM and thrombocytopenia due to viral infection. The patient was then given a 1,700 kcal DM diet with the oxygen of 10L/min via a non-rebreathing mask, injection of

Levofloxacin 750mg/24 hours, drips of acetylcysteine 2,500mg (12.5 ml) via syringe pump 3cc /hour/day, injection of methylprednisolone 40mg/12 hours for 3 days, azithromycin tab 1x500mg, oseltamivir tab 1x500mg, Vit B Comp tab 3x1, Vit C tab 3x500mg and Zinc tab 1x20mg.

On the next day, the patient's throat swab confirmed a positive COVID-19 result, fasting blood glucose of 230 mg/dL, a 2-hour postprandial blood glucose of 245 mg/dL, HbA1c of 11.7%. The patient was then diagnosed with a moderate degree confirmed COVID-19 with DM and was given additional insulin injection therapy (Aspart insulin 6-6-6 U/SC and Glargine Insulin 0-0-12 U/SC). The patient was then screened daily of fasting blood glucose and 2-hour postprandial for monitoring blood glucose levels. Nevertheless, as the patients still demand an injection of methylprednisolone, the patient's glucose level is challenging to control, and finally, intravenous insulin administration was started via the syringe pump. Drips of insulin (Aspart insulin) 50IU in 50cc of normal saline starting at 3cc/hour via a syringe pump with blood glucose monitoring done hourly. The dose of insulin was adjusted according to the patient's blood glucose to maintain a fasting blood glucose level 100 to 140mg/dL and a 2-hour postprandial blood glucose level of 140 to 200mg/L.

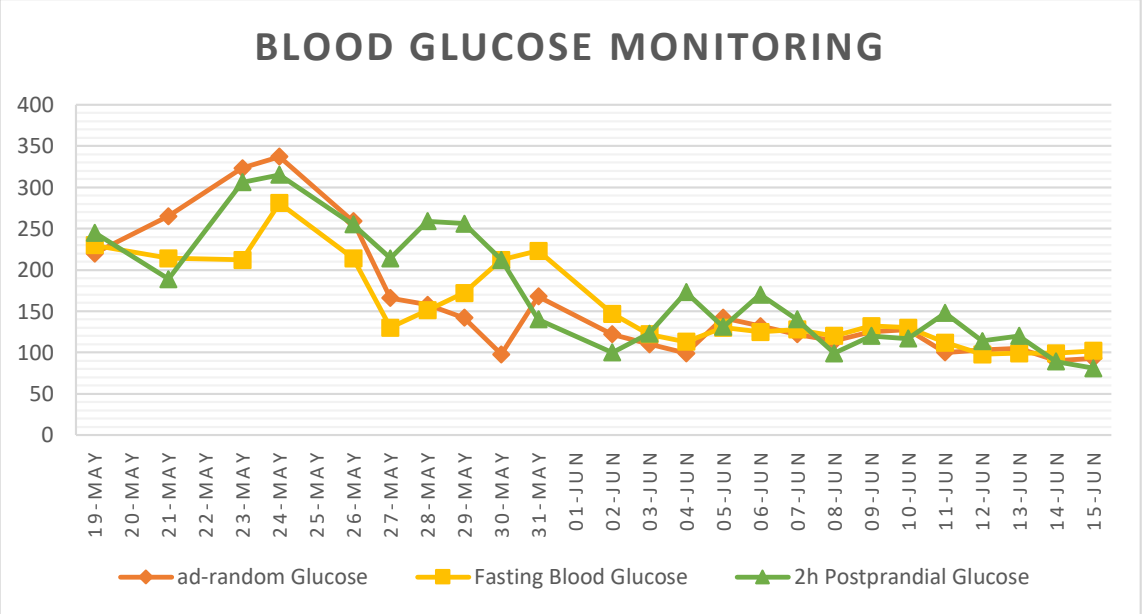

Figure 3. Changes trends of blood glucose in the patient. This figure showed that the patient's blood glucose was high and fluctuated significantly at the time of hospital admission, and that the blood glucose stable at normal level when discharged.

On May 27, 2020, as the patient's blood sugar began to preserve, insulin administration via the syringe pump was suspended and subcutaneous insulin injections were presented again. After a comprehensive glycemic control and blood glucose monitoring, the patient's blood glucose gradually stabilizes (Fig. 3). The patient was then discharged from the hospital on 22 June 2020, after 2 consecutive negative throat swab tests for COVID-19, blood glucose levels were normal, and achieved stable states.

3 Discussion

COVID-19 can affect all ages, however, the elderly and people who have a history of chronic disease (co-morbid) are at greater risk and with worse complications from this disease. Specifically for those with DM, it is the second most common comorbidity found, in about 8% of cases, after hypertension, and with a triple death rate compared to sufferers in general (7.3% versus 2.3%) [3]. It is important not to underestimate the severity of COVID-19 in patients with DM, even in the absence of alarming classic signs and symptoms, and may be useful for developing different clinical severity scores for patients with diabetes [4].

Plasma glucose and DM levels are independent predictors of mortality and morbidity in patients with SARS. Potential mechanisms that can increase susceptibility to COVID-19 in patients with T2DM include: (1) cellular binding with higher affinity and efficient virus entry, (2) decreased viral clearance, (3) reduced T cell function, (4) increased susceptibility to inflammation and cytokine storm, and (5) presence of cardiovascular disease (CVD) (Fig. 4) [6, 7].

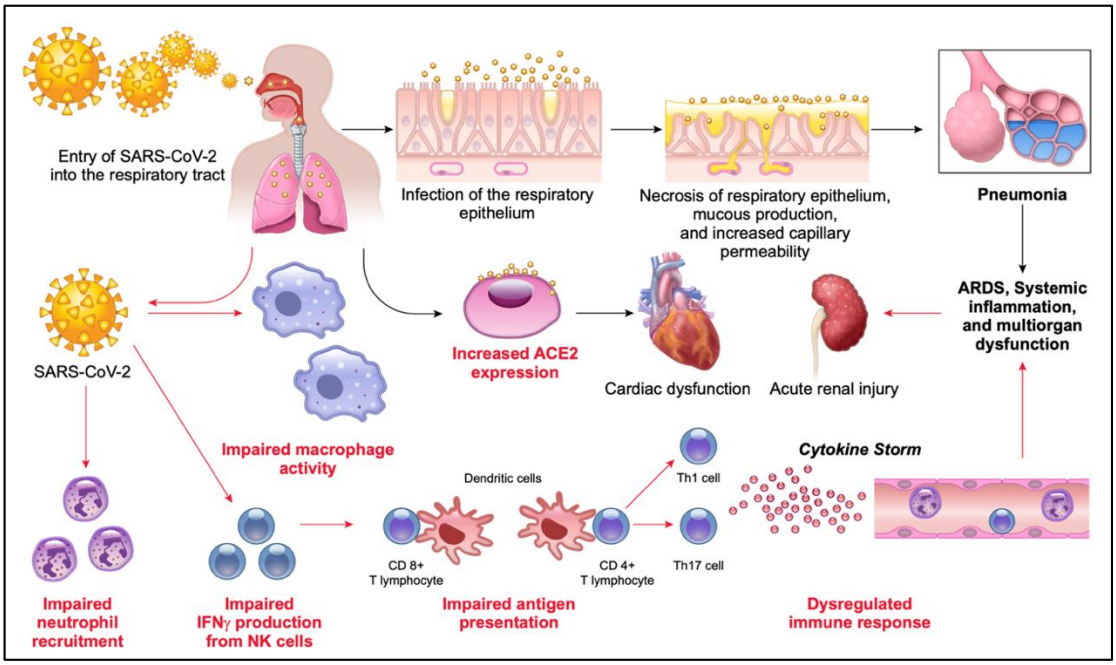

Figure 4. Mechanisms of increasing susceptibility to COVID-19 in patients with diabetes mellitus (DM) (R. Muniyappa and S. Gubbi, 2020) [16]

S-glycoprotein on the surface of SARS-CoV-2 binds to ACE-2 and causes conformational changes in S-glycoprotein. This allows proteolytic by host cell proteases (TMPRSS2 and Furin) to eventually lead to the internalization of virions. The entry of viral cells triggers an inflammatory response by recruiting T-helper cells that produce interferon G and will attract other inflammatory cells that lead to cytokine storms that can cause people damage and multi-organ failure. Additionally, some are responsible for increasing the risk and severity of infection with SARS-CoV-2 in diabetes: (1) increased expression of ACE-2: in an experiment in diabetic rats, there was an increased expression of ACE-2 in the renal cortex, liver, and pancreas, (2) furin increase:

where protease is bound to type 1 membrane, which is included in the proteinases subtilisin convertase, (3) impaired T cell function: where changes occur in CD4 lymphocytes, and (4) increased Interleukin-6 (IL-6). [2, 5]

Diabetes mellitus inhibits neutrophil chemotaxis, phagocytosis, and intracellular microbial killing. Adaptive immunity disorders are characterized by an initial delay in activation of Th1-mediated immune cells and an advanced hyperinflammatory response is often observed in patients with diabetes [2, 6, 8]. In patients with COVID-19, peripheral CD4+ and CD8+ T cell counts are low, but with a higher proportion of Th17 CD4+ proinflammatory T cells, and elevated cytokine levels. Thus, patients with DM might weaken the IFN anti-viral response, and the delayed activation of Th1/Th17 can contribute to an increase in the inflammatory response [6, 9, 10].

Hyperglycaemia and insulin resistance increase the synthesis of glycosylated end products (AGEs) and pro-inflammatory cytokines, oxidative stress, in addition to stimulating the production of adhesion molecules that mediate tissue inflammation [11, 12]. This inflammatory process can devise underlying mechanisms that lead to a higher tendency for infection, with worse outcomes in patients with diabetes [1, 11].

Meanwhile, uncontrolled diabetes is correlated with inhibition of lymphocyte proliferation response to various types of stimuli, as well as impaired monocyte/macrophage and neutrophil function. Abnormal delayed hypersensitivity reactions and complement activation dysfunction have also been described in patients with diabetes. In vitro studies show that exposure to pulmonary epithelial cells with high glucose concentrations significantly increases infection and replication of influenza viruses, which suggests that hyper glycemia can increase viral replication in vivo. [1, 11, 13]

So far there has been no officially approved drug or anti-SARS CoV-2 vaccine for COVID-19 treatment, in several ongoing clinical trials. The specific aspects of diabetes management with COVID-19 include: (1) Metabolic and glycaemic control, essential in patients with COVID-19. Patients with poor glycaemic control enhance the risk of complications and death. Doses of antihyperglycemic drugs may have to be adjusted depending on blood glucose levels. Most patients who are hospitalized with COVID-19, especially those with respiratory problems, will need insulin. Ideally, patients with very poor oral intake or those who use mechanical ventilation require intravenous insulin infusion with regular blood glucose monitoring. This includes continuation and strict abidance with adequate control of blood pressure and lipids. (2) Blood Glucose Monitoring, blood glucose monitoring poses particular challenges, primarily if the patient is critically ill and is receiving intravenous insulin. If the patient is not critically ill, the patient can be given a glucose test kit and self-monitoring can be taught. (3) Monitoring of electrolytes, pH, blood ketones, or β-hydroxybutyrate [5,14,15]. Given the potentially devastating effects of hyperglycaemia and ketosis on multi-organ function, intensive monitoring and insulin

therapy should be essential for the advancement of results in diabetic patients with SARS-CoV-2 infections. [16]

The use of steroid treatment in people with pre-existing diabetes will undoubtedly result in worsening glucose control; termed as steroid induced hyperglycemia. This will warrant temporary additional and more active glycaemic management. There is little evidence to guide how patients with hyperglycaemia related to steroid use should be managed. The control goals are those recommended for most patients with diabetes mellitus: pre-prandial glycemia [17,18].

Control of hyperglycaemia will improve symptoms, reduce risk of acute complications, and reduce increased risk of infection and other complications associated with hyperglycaemia. Subcutaneous insulin using a basal or multiple daily injection regimen will be the most appropriate choice of treatment to achieve glycemic control. For patients with persistent significant hyperglycemia with glucose levels >300 mg/dL, more aggressive insulin therapy is indicated, such as intravenous insulin infusion, a higher dose of insulin, or more frequent correction with rapid-acting insulin. Close attention will need to be paid to blood glucose monitoring and early intervention may be necessary to prevent prolonged symptomatic hyperglycaemia. Consequent titration of the insulin dose will allow maintenance of glucose control in the face of increasing or decreasing steroid dose [17,18].

4 Conclusion

We have reported a case of confirmed COVID-19 patient with newly diagnosed diabetes mellitus. This case showed that the comprehensive glycaemic control and blood glucose monitoring accomplished good treatment effects on a COVID-19 patient with diabetes.

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