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Literature Review

The risk factors of diabetes mellitus towards Covid-19's outbreaks

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ABSTRACT

Covid-19 patients with Diabetes mellitus (DM) ranked third after hypertension and cardiovascular disease with an estimated 36% of all Covid-19 cases. These patients have a risk of experiencing a higher complication possibility since their metabolic disorder can cause hyperglycemia to the patient. It is showed that the number of deaths reached 7,3%, which is higher than non-diabetes. The increase of DM patients caused by stress factors may trigger the onset of glucose in blood sugar, and the glucose variability became abnormal. This circumstance may cause a glycemic increase that causes the predisposition intensification of susceptible affected by Covid-19. Good management is truly needed for DM patients affected by Covid-19. It is hoped to reduce the risk factor, such as preventing complications and increasing life quality by regular medical check to have a good prognosis. Some research showed that Covid-19 patients with DM are essential in ICU and need more treatment attention as they may experience Acute Respiratory Distress Syndrome (ARDS). Diabetes mellitus patients' treatment strategy is to manage the blood glucose level, especially in post-prandial glucose. This literature aims to know the degree of serious illness of Covid-19 patients by the comorbidity of DM in this pandemic event.



INTRODUCTION

Coronavirus is the class of Coronaviridae that has layered by RNA's genome with a large strand secured by polyadenylated (Van Der Hoek et al., 2016). Coronavirus's shape could be a circle secured by the pleomorphic shape. It also comprises glycoprotein that encompassed the center, which comprises a protein lattice with the single structure of RNA interior. This structure is related to nucleoprotein, a glycoprotein that has the capability to connect to the have additionally as the most antigenic (Guo et al., 2020).

The clinical manifestation may appear in 2-14 days after infected the exposure sign and symptoms, for example, having a fever of more than 37°C, fatigue, and dry cough. In some cases, the patient may also experience an ache and pain, nasal congestion, cold, tightness, sore throat, or diarrhea. The risk factor of those who may be affected is in the age of 60 years above, male, have comorbidities disease, chronic pulmonary disease, kidney disease, and diabetes disease medical record (WHO, 2020). The incubation time of Coronavirus is described as the first phase of infection until the appearance of symptoms/disease. As mentioned from some studies in China, the incubation time average is five days, and the symptoms increase at 97,5% in 12 days (Hussain, Bhowmik, & do Vale Moreira, 2020). The prognosis of COVID-19 is some patients that have a mild infection is not necessary to do hospitalization. Meanwhile, patients who are hospitalized are 10%-20% in ICU, 3%-10% need intubation, and the rest 2%-5% died (Tinku, 2020).

Diabetes Mellitus is a metabolic disorder characterized by hyperglycemia due to the occurrence of insulin disorders (Goldenberg & Punthakee, 2013). Based on the International Diabetes Federation (IDF), the prevalence of Diabetes Mellitus in the world is 1.9% and ranked the seventh leading cause of death

in the world. In 2013, the number of Mellitus cases in the world reached 382 million. The proportion of events Diabetes Mellitus type 2 is 95% of the world population and became prevalence Diabetes Mellitus type 2 in the number of 85%-90% (Saeedi et al., 2019). The signs and side effects of Diabetes Mellitus may show up as frequent urination, intemperate thirst, inconsequential weight loss, extraordinary starvation (polyphagia), shivering (paranesthesia) or deadness in hands or feet, weariness, exceptionally dry skin (xerosis), and on the off chance that there's a contamination, the bruises are moderate to recuperate (CDC, 2016) The prognosis of Diabetes Mellitus itself depends on the patient condition and their discipline to consume the prescribed medication (Hill, Mantzoros, & Sowers, 2020).

The COVID patient with Diabetes Mellitus disease showed a higher risk of complication or death. In the Intensive Care Unit of COVID, 22% of patients have Diabetes Mellitus medical records. The report summary from China showed that 72.314 cases of death increase to 7,3% to Diabetes Mellitus patients with the comorbidity Diabetes of death patients to 2,3% compared to the Cardiovascular and Hypertension (Hill et al., 2020).

Diabetes Mellitus also reported as one of the comorbidities to COVID-19 patients since it is found the worse number of mortality and significantly can make the patient's condition severe related to the age and the uncontrolled Diabetes Mellitus. The number of mortalities, in this case, is varied in each country and age group from the affected patient. In the case of diabetes patients, there is an increase of 7,3% of comorbidity comparing to the general people, which is only 2,3%. The Diabetes condition can make the patient's condition severe since the disorder of immune is experienced. The prognosis is diagnosed may be severe because of organ failure, acute respiratory disorders, and the last septic shock of the patient that



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experienced the disorder (Baidya et al., 2020)

Many theories have been proposed to explain the risk factor of diabetes mellitus toward Covid-19 outbreaks. Although the literature covers a wide variety of such theories, it is difficult to know the factor that aggravates DM in Covid-19 comorbidities. We conducted a systemic literature review of the risk factor of diabetes mellitus toward Covid-19 outbreaks to better understand the distribution of pathogenesis specific of Diabetes Mellitus in Covid-19 patients. To our knowledge, this is the systemic review designed for the data from multiple pathogens which might be applied to annual incidence.

RESEARCH METHODS

The method used is to collect and analyze research articles related to Covid-19 patients with Diabetes Mellitus morbidity. Articles were obtained through searches using Google Scholar, PubMed, and Elsevier electronic databases using the keywords Covid-19, Sars Cov-2, risk factor, and Diabetes Mellitus. The articles reviewed are all articles published from 2010-2020 that discuss Covid-19 in full-text format, where the specifications discuss Covid-19 patients with Diabetes Mellitus comorbidity.

Table 1. Research Summary on The Risk Factor of diabetes mellitus towards covid-19's outbreaks

Author; Years	Type of Literature	Conclusion According to PICO
Singh, Gupta, Ghosh, & Misra, 2020a	<i>Study Case</i>	Diabetes is associated with an increase in the incidence of severity of Covid-19. It is important to control blood glucose in patients infected with Covid-19.
Bornstein et al., 2020a	<i>Literature review</i>	Care management of Diabetes Mellitus patients with Covid-19 infection is certain. In patients with DM are expected to continue to regulate lifestyle and take primary prevention in order to avoid complications.
Orioli et al., 2020	<i>Clinical Research</i>	Patients with Diabetes Mellitus type 1 should often do checking blood glucose and ketone urine at the time of fever. Drug doses and corrective bolus are necessary to maintain normoglycemia.
Saeedi et al., 2019	<i>Experimental Study</i>	Patient with Diabetes Mellitus infected with Covid-19 must regulate stress levels related to the presence of self-isolation during the pandemic and regulate physical activities due to reduced physical activity to worsen the glycemic state and blood pressure, thus making patients vulnerable to Covid-19



Continued from Table 1.

Author; Years	Type of Literature	Conclusion According to PICO
Hill et al., 2020a	<i>Study Case</i>	Diabetes Mellitus patients who are infected with Covid-19 but do outpatient required self-awareness to take drugs adequately and conduct glycemc examinations regularly and carry out routine controls
Jiang, 2020	<i>Article in Press</i>	The incubation period of Covid-19 is 1 to 14 days and generally 3 to 7 days. The treatment includes isolation, symptomatic, support, and close monitoring of condition change; the critical case should be admitted to the ICU as soon as possible
Shereen, Khan, Kazmi, Bashir, & Siddique, 2020	<i>Literature Review</i>	The novel coronavirus originated from the Hunan seafood market at Wuhan. DNA recombination was found to be involved at spike glycoprotein, which assorted SARS-COV with RBD of another Beta Cov.
Muniyappa & Gubbi, 2020	<i>Study Case</i>	In experiments using mice, ACE-2 aims to understand how hyperglycemia, hyperinsulinemia, and hypoglycemic agents affect
Di Gennaro et al., 2020	<i>Study Case</i>	efficacy of vaccines and antiviral investigation agencies. People with Covid-19 require self-isolation; among others, patients who are recommended to have follow-up examinations can be the main symptoms and have a history of traveling to cities exposed to covid-19
Katulanda et al., 2020	<i>Study Case</i>	Guidelines for the Treatment of Diabetes Mellitus with Covid-19 infection still do not get adequate drugs so until now conduct clinical trials while the safety of management needs to be considered safe with relative advantages



LITERATURE REVIEW

EPIDEMIOLOGY

The Covid-19 pandemic was starting to spread widely at the beginning of December in Wuhan, the 7th most populous city in China. The first confirmed Covid-19 case outside China is on 13 January 2020 in Bangkok. On 2 March 2020, 67 areas outside China had been reported in 8565 confirmed cases with the number of deaths of 132 people. It was also found the significant spread of the virus in some countries, including Iran and Italia, which has been stated as a global pandemic by WHO on 11 March 2020. The number of confirmed cases is to keep increasing all over the world in Europe and Asia. By 31 March 2020, WHO reported there are 693.224 confirmed cases globally and found 33.106 deaths that are divided into some region, Western Pacific 103.775 cases with 3649 deaths, Europe 392.757 cases with 29.962 deaths, South-East Asia 4084 cases with 184 deaths, Eastern Mediterranean 46.329 cases with 2813 deaths, America 142.081 cases with 2457 deaths, and Africa 3486 cases with 60 deaths (Rothan & Byrareddy, 2020).

World Health Organization (WHO) predicts that the number of Diabetes Mellitus patients in Indonesia was 8.4 million in 2000, then becomes 21.3 million in 2030. The International Diabetes Federation (IDF) also predicts the increasing number of Diabetes Mellitus patients in Indonesia from 9.1 million in 2014 to 14.1 million in 2035. Based on IDF data in 2014, Indonesia ranked in the 5th position globally, which has increased two times in 2013, with 7.6 million Diabetes Mellitus patients (Rahmadi, 2019). The research conducted by Onder et al., 2020 in Italia showed that the Diabetes Mellitus patient with Covid-19 case reached 36%, meanwhile in the United States of America reported about the Covid-19 patient with Diabetes Mellitus reached 58%. The response team of Covid-19 from the Centre

for Disease Control (CDC) reported that the prevalence is 11% of 7.162 COVID patient data (CDC, 2016) stated in his research that he found the Covid-19 patient with comorbidities, including Diabetes Mellitus, required to be in ICU. The patient with Diabetes Mellitus clinical record has a chance of Acute Respiratory Distress Syndrome (ARDS) intricacy. The study in the Philippines had resulted that 55% of COVID-19 patients with Diabetes Mellitus got a bad prognosis and resulted in a worse number of deaths and complications (Singh et al., 2020).

PATHOPHYSIOLOGY

Pathophysiology of Covid-19

Coronavirus contains specific gen, which is ORF1, to do transmigration that works to give codes to protein so that there will happen a virus replication and nucleocapsid formation. The glycoprotein in the outer surface of the virus has a function to attach and enter the virus into the main cell and build Domain Receptor Binding (RBD) that can loosen up and attach to the virus. Some of the Coronavirus take back the aminopeptidase or carbohydrate as the key to enter the human body. The mechanism of Coronavirus entering the human body is based on the cellular protease that consists of Human Airway Trypsin Like Protease (HAT). The cathepsin and transmembrane protease serine 2 (TMPRSS2) will break the protein and form penetration. The Coronavirus has a typical structure with protein. The increment of protein in Coronavirus contains a 3D structure to maintain Van Der Waals (Shereen et al., 2020).

Pathophysiology of Diabetes Mellitus

The insulin resistance of muscle and liver and also pancreatic beta-cell failure has made the central pathophysiology failure in Diabetes Mellitus in the condition of beta-cell failure. Besides occurring in the muscles, liver, and



beta cell, it also occurred in fat tissue (lipolysis increase), gastrointestinal (incretin deficiency), alpha pancreas cell (hyperglucagonemia), kidney (glucose absorption increase), and brain (insulin resistance) in diabetic organs that can cause the glucose tolerance disorder on Diabetes Mellitus (Soelistijo et al., 2015). The pancreatic beta cells cannot produce insulin secretion at high speed to balance the insulin resistance, insulin sensitivity disorder, and insulin secretion since it must occur altogether before glucose intolerance happens at the same time. This condition caused late insulin secretion that is enough to reduce the glucose level in peripheral tissue, fat tissue, and muscle tissue. The prandial glucose fluctuation is also considered as the determinant in setting the glucose fluctuation daily. The condition of high post-prandial glucose can cause long-term diabetic complications. The post-prandial glucose fluctuation can be the determiner to measure HbA1c level, especially after eating lunch. Otherwise, Hb1Ac becomes the determiner of progressive diabetic complications (Tjandrawinata, 2016).

Pathophysiology of Diabetes Mellitus with Covid-19

Uncontrolled Diabetes and glycemia are reported to be significant predictors with severity and mortality in patients affected by viral infections. The Covid-19 patient with Diabetes Mellitus record can experience higher stress level conditions that can trigger the hormone release, which causes hyperglycaemic, for example, glucocorticoid and catecholamines. Those conditions can increase glucose level and abnormal glucose variability (Hussain et al., 2020). They could also encounter a decrease of the immune response towards the infection related to the cytokines and the immune response change, including T-cell and macrophages. In China, several Diabetes Mellitus patient has an inadequate metabolic control which makes

them susceptible to Covid-19 infection (Zhang et al., 2020).

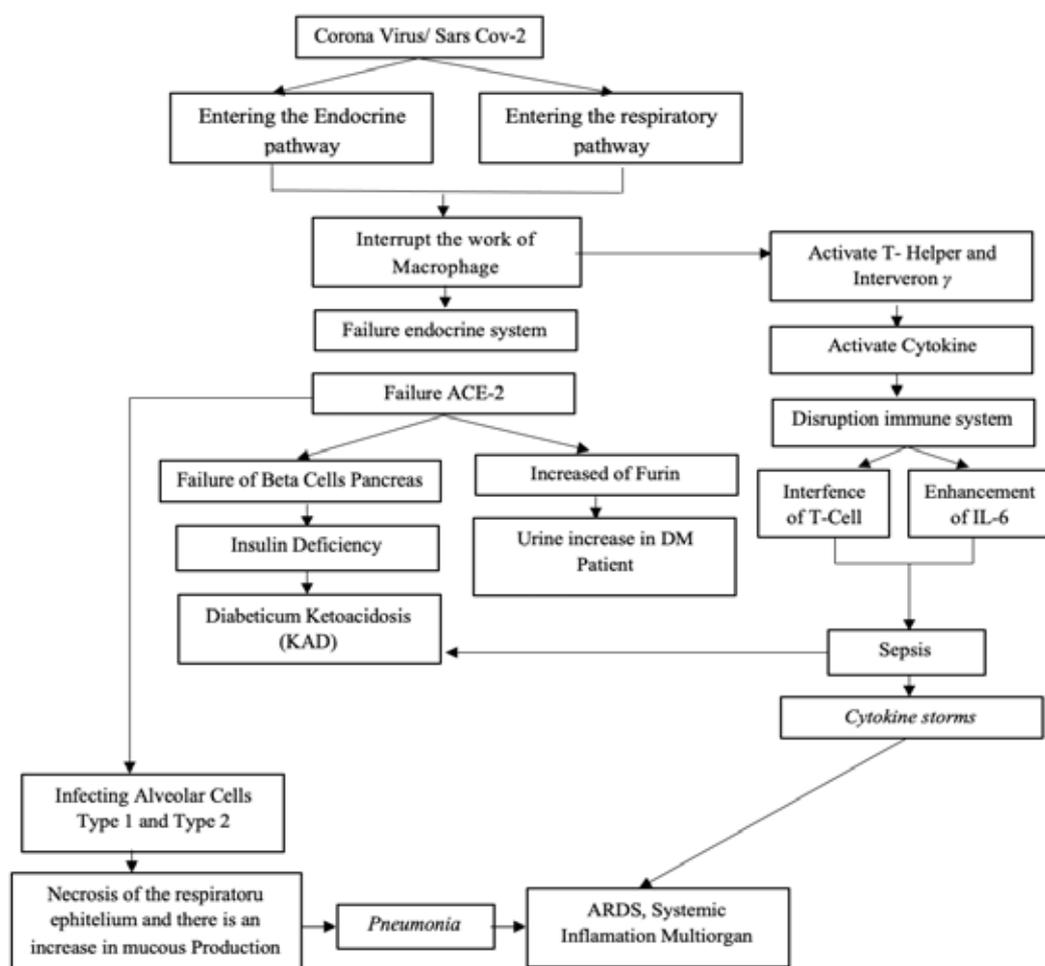
Coronavirus uses ACE-2 as the receptor to enter the alveolar epithelial cells type I and II in the lungs and the heart, endothelium, epithelial of the kidney, digestive tract, and pancreas. The S-glycoprotein will connect to Coronavirus. The virus that enters the cell generates an inflammation response by using a T-helper that activates interferon γ , which will make the cytokines active. This condition can cause organ damage, and also the failure of related organs to the kidney will increase ACE-2 activity in the kidney's cortex, liver, and pancreas. The increase of urine production of the Diabetes Mellitus patient is obtained by the protease type-1 that is related to membrane cell and causes the Coronavirus replication faster. The T-cell function disorder can cause lymphocytopenia and will lead to a patient's prognosis. The increase of Interleukin-6 (IL-6) has a role as a destroyer of Covid-19 infection but still under research (Baidya et al., 2020). Angiotensin-Converting Enzyme 2 (ACE) is the surface receptor of Coronavirus's surface, which directly interacting with S-Glycoprotein (Protein S). The research mentioned that ACE has a role as the binder domain receptor of Coronavirus that later will be spread to certain organs and cause the patient of Covid-19 to die because of organ failure (Weina et al., 2020).

Two specific mechanisms will play a role in the Covid-19 infection of Diabetes Mellitus patients. Firstly, the SARS Cov-2 virus starts to broke the endocrine track in charge of arranging blood pressure, metabolism, and inflammation. The Coronavirus will disturb ACE-2, which will induct cell failure, hyper inflammation, and respiratory failure (Bornstein et al., 2020b). Diabetes Mellitus patients with hyperglycemia will experience the ACE-2 increase that can facilitate the virus to enter. However, it will reduce the ACE-2 level in chronic hyperglycemia conditions and

cause inflammation and virus failure. The β -cell failure can cause insulin deficiency, which may cause Diabetic Ketoacidosis (DKA) (Chen, Li, Chen, & Li, 2020). Secondly, it is related to the dipeptidyl peptidase-4 (DPP-4) enzyme. The DPP-4 has a function as a functional receptor for Human Coronavirus Erasmus Medical Center (hCov-EMC) it is a glycoprotein transmembrane type II that has an important role in glucose metabolism and insulin and can increase the inflammation of Diabetes Mellitus type II inflammation (Van Der Hoek et al., 2016).

The DPP-4 is oligopeptide, a tissue that is involved as the activation of growth factor and as the activation T-cell peptide as the glucose metabolism controller (Shereen et al., 2020). The patient of Diabetes Mellitus, hyperglycemia, and insulinogenic can weaken proinflammation cytokine synthesis functionally by damaging the immune system and human host in long-term conditions. It can damage metabolic disorder, damage macrophage function, and lymphocytes that caused an individual more susceptible to complications (Lu, Gu, Zhang, Liu, & Ning, 2020)

Figure 1. The mechanism is expected to have a contribution to the susceptible increase of Coronavirus (COVID-19) disease in Diabetes Mellitus patient





DIAGNOSIS

The COVID patient case is divided into three classifications. The first is patient under observation; which is a person that experiencing symptoms of fever ($\geq 38^{\circ}\text{C}$) or having a fever medical record and symptoms like cough, cold, sore throat, mild to severe pneumonia, and also arrived from some affected countries in the last 14 days after experiencing the symptoms or patients with acute respiratory infections with mild severity as severe and have been in close contact with patients with confirmed or probable cases of Covid-19, worked or visited health care facilities with confirmed cases in areas/countries affected by Covid-19, have a history of travel to countries affected by Covid-19 and have a fever. The second is persons under surveillance, which is a person that experienced a fever or the medical record of fever or upper respiratory tract infection (URI) without pneumonia and arrived from some affected countries in the last 14 days before experiencing the symptoms and does not have one or more exposure histories including a history of close contact with Covid-19 confirmed cases, Probable cases are patients under supervision who are examined for Covid-19 but are cannot be confirmed that a person with positive confirmation results of pan-coronavirus or beta-corona virus. The case can be categorized as positive if the patient infected by COVID-19 has been tested by the laboratory by using the PCR swab test twice, and both have resulted positive (Singh et al., 2020a). The incubation time of Coronavirus is described as the first phase of infection until the appearance of symptoms/disease. As mentioned from some studies in China, the incubation time average is five days, and the symptoms increase at 97,5% in 12 days (Hussain et al., 2020).

The prognosis of COVID-19 is some patients that have a mild infection is not necessary to do

hospitalization. M. The prognosis of Covid-19 is some patients that have a mild infection is not necessary to do hospitalization. Meanwhile, hospitalized patients are 10%-20% in ICU, 3%-10% need intubation, and the rest 2%-5% died (Hill, Mantzoros, & Sowers, 2020b).

The diagnosis of Covid-19 can be made by doing some tests, such as rapid test, PCR, radiology of thorax photo, CT-Scan, and thorax USG that have a result of bilateral opacity subsegmental consolidation, lobar or lungs collapse or nodule, and ground glass image. In the early stage, it shows a small plague with the interstitial change that shows in lungs peripheral and develops to multiple shadows of ground glass and also found the existence of infiltrate in both lungs. In the serious case, it is found the existence of "white-lung" (Shi et al., 2020). The radiographic image captured on Covid-19 patient from CT-scan is found that the compromised unilateral image (53%), ground-glass opacification (93%), the thickening of the interlobular septum and pleura, nodule exist, and bronchiectasis (Shi et al., 2020).

The antigen base examination has a function to detect protein virus (antigen) in the respiratory tract sample. The antigen will tie a certain antibody and will result in a visual sign. The duplicate antigen will react when the virus is active in doing duplication (WHO, 2020). Doing RT-PCR examination on the suspected patient of Covid-19 is essential, especially for those who feel pneumonia or serious illness and shortness of breath. If the RT-PCR is not available, it can be examined by doing a serology check. Besides, the Bronchoscopy check is also possible, along with the pleura function and blood test (Mardani et al., 2020). In the PCR test, those are needed to have a sensitivity level of 69% in IgM and 93.1% in IgG. Some PCR tests resulted in "true positive" which means the COVID patient still has not developed the specific virus antibody to have a more sensitive result of IgG. A further Immunosorbent assay



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enzyme (ELISA) test is needed since it has a higher sensitive test in 97.5% (Hoffman et al., 2020).

In Diabetes Mellitus suggested test is to check the glucose enzymatically by using vena blood plasm, which resulted in a specific symptom and also the plasma glucose random $>200\text{mg/dl}$, plasma glucose fasting $>126\text{mg/dl}$ can prove the diagnose of Diabetes Mellitus, there are some methods in conducting tests for Diabetes Mellitus patients that have a certain purpose, for example, diagnostic tests and filter test. The diagnostic test is conducted for patients who have Diabetes Mellitus symptoms and filter tests for those who have no symptoms but are included in the risk factor of Diabetes Mellitus. The characteristics are more than 45 years old, obesity, hypertense, family history of Diabetes Mellitus patients, cholesterol HDL $\leq 35\text{mg/dL}$, or triglycerides $>250\text{mg/dL}$ If the condition of blood sugar level 2 hours of TTGO $> 200\text{mg}$, it uses glucose load that is equal to 75 grams of glucose dissolved in water (Fatimah, 2015). The Diabetes Mellitus patient that is infected by Covid-19 at the examination will find the existence of lymphocytopenia, thrombopenia, and leukopenia. The next stage is found in the increase of pro-inflammatory cytokines, including IL-6 and C-reactive protein. After that, the result discovers the increase of insulin resentences with endothelial failure. The chronic patient will show the existence of vascular (Hussain et al., 2020).

The glucose level of Diabetes Mellitus tolerant turns into the free indicator factor that can build the likely contamination of Coronavirus it comprises of the decline of white blood cell work, and CVD positive which causes Diabetes Mellitus patient to have the chance of IFN cumulation and to diminish of TH1/TH17 reaction that adds to aggravation reaction so it can build the inconvenience hazard (Muniyappa & Gubbi, 2020). Patients with Covid-19 comorbidities Diabetes Mellitus can be a dangerous condition

because of hyperglycemia, insulin tolerance, and obesity. The Coronavirus comorbidity with Diabetes Mellitus issue has an all the more clear depiction, for instance, the extension of exacerbation biomarker [C-responsive protein (CRP) and Interleukin 6 (IL-6) and (IL-1)], the addition of synthetic [Lactate Dehydrogenase (LDH)], and coagulation issue (D-dimer) and Tumor Necrosis Factor-alpha (TNF- α) (Huang, Lim, & Pranata, 2020). Those issues are related to certifiable multi-organ dissatisfaction and tend to thrombotic events in like manner "Cytokine Storm" will make the Coronavirus outrageous (Orioli et al., 2020).

THERAPY

The treatment in Diabetes Mellitus tolerant with Covid-19 has an intent to diminish the chance of hyperglycemia since the ordinary glucose level will lessen the microorganisms improvement danger in pneumonia conditions (Singh, Gupta, Ghosh, & Misra, 2020b). For this reason, there are some managements to do such as doing exercise (3-4 times a week for 30 minutes), implementing a Diabetic Diet by counting basal calorie as 25-30 calorie/kg of ideal weight for an obese patient, making calorie reduction 20-30% from basal calorie, Mediterranean Diet is a diet by doing a plant-based diet as a glycemic controller and reduce the risk factor (Rahmadi, 2019).

In type 2 Diabetes Mellitus (T2DM) patients, the Metformin and Inhibitor SGLT-2 dose is needed to be stopped since metformin has antiproliferative characteristics and immunomodulator works as AMP-activated protein kinase inhibitors. The metformin function also reduces the death risk of patients with chronic respiratory system symptoms. The dipeptidyl peptidase 4 (PDP-4) inhibitor and also linagliptin can be used so kidney disorder and hypoglycemia will not occur. The DMT2 patient needs to have insulin treatment.



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For those who already get treatment of insulin in basal, they need to have the bolus insulin treatment as well to reduce the risk factor of hyperglycemia (Jia et al., 2019). The patient with hyperglycemia condition can affect the lung's function so they can experience a state of pulmonary dysfunction which led the virus to do duplication easily (Hill et al., 2020a). Suppose the patient has a glucose metabolism disorder and is in critical condition. In that case, they need to be given intravenous insulin, which aims to fix water disorder, electrolyte, and pH balance (acid-base balance) which refers to Diabetes ketoacidosis. Diabetes Mellitus patients with fever can be given glucocorticoid and insulin therapy. If the patient in critical condition, there some suggested medications such as acetaminophen, atenolol, and lisinopril (Ma & Ran, 2020).

In type 1 Diabetes Mellitus (T1DM) patients, they need to have blood glucose and urinary ketones frequently test if they feel a fever with hyperglycemia. Therefore, dosage change is needed to maintain normoglycemia (Bornstein et al., 2020b). They also need insulin pump therapy with the insulin dosage given is by monitoring the glucose and ketones to avoid glycemia in patient's decrease food intake. This treatment also works effectively to avoid serious hyperglycemia and ketoacidosis (Baidya et al., 2020).

The mechanism of Coronavirus itself is by doing isolation for the patient, symptomatic treatment, monitoring the patient intensively, and doing oxygen saturation measurement through the respiratory tract or by the oximeter. The dosage usage of ribavirin becomes 500 mg for adults in two until three times a day through an intravenous (Jiang, 2020). Giving Lopinavir/ Ritonavir also can decrease by 50% of Coronavirus duplication. Ribavirin and Oseltamivir can also be given along with ACE-inhibitor

such as interferon, Chloroquine, Tocilizumab (optional), corticosteroid, and also the anti-bacterial therapy if the patient of Covid-19 has suffered pneumonia. Chloroquine was accepted in 2014 as the additional medicine for diet by the Drugs Controller General of India (DCGI) as the medicine that can increase glycemic control in T2DM and also showed a significant effect for Covid-19 patients (Jia et al., 2019).

The Covid-19 patient with Diabetes Mellitus, which is in the Intensive Care Unit (ICU), needs to be monitored, especially the plasm glucose, electrolytes, pH, blood ketones, or beta-hydroxybutyrate, and insulin therapy intravenously. In the case of ARDS and hyper inflammation, for proper titration, high insulin management is given, and the subcutaneous insulin infusion can be an option and have some advantages (Bornstein et al., 2020b). The inpatients need to be given insulin therapy subcutaneously by giving once or twice a day along with the eat time bolus so the insulin will work faster or slower. This kind of strategy is one of the glycemic management. The metformin dosage must be stopped if lactic acidosis happened (Katulanda et al., 2020). It is necessary to do glycemic control since this is having an important role for the Diabetes Mellitus patient with Covid-19 since the control management can decrease complication risk and death numbers. For inpatient who suffers a mild infection, the therapy is given antihyperglycemic orally, yet it is also suggested inhibiting SGLT-2 because it has dehydration risk. The euglycemic ketosis and metformin dosage need to be stopped if the patient vomiting or have cannot have oral sulfonylurea intake and the dosage of insulin need to be changed based on the blood glucose, a special strategy for Covid-19 with Diabetes Mellitus patient is by managing the blood glucose especially the post-prandial. The patient must diet, and those who in quarantine are not allowed to exercise in a small room since they have a bad pulmonary



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function to overcome their anxiety that may lead to hyperglycemia. The patient also needs to consume medicine routinely since the pancreas is the potential target of the virus that can affect glucose metabolism (Jia et al., 2019).

CONCLUSION

Diabetes Mellitus patients have a higher risk of being infected by the Covid-19 virus. They also have a higher risk to experience a complication along with death. The patient's self-isolation must be carried out because this action can increase the stress level, which may lead the glycemia to increase and predispose the patient to be susceptible to be infected by Covid-19. The methods conducted to diagnose Covid-19 are Rapid Test, PCR Test, Radiology check of Thorax image, CT scan, and Thorax USG. The primary purpose of therapy for Covid-19 patients with Diabetes is to decrease the hyperglycemia occurrence so it will not increase the possibility of complications of the patient. The dosage of Metformin and SGLT-2 need to be stopped in the long term since it may cause a hypoglycemia effect to the patient.

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