



COVID-19 and Diabetes Mellitus; An Overview

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ABSTRACT

Diabetes Mellitus (DM) is a long-term metabolic disorder that affects many organs in the body. Diabetes may be linked to a serious type of Coronavirus Disease in 2019 (COVID-19). COVID-19 will make people with diabetes three times more likely to become seriously ill or die. They discovered that advanced age, obesity, and other medical conditions linked to diabetes are also associated with increased risk. In the countries hardest hit by the pandemic, increased morbidity and mortality from COVID-19 in diabetic patients have been observed, and this link, as well as the best management of infected diabetic patients, deserve further investigation. Anti-diabetic medications that can minimise inflammation while maintaining good glycemic control are ideal. Patients admitted to the hospital with extreme COVID-19 can need changes to their diabetes care, such as stopping current medications and starting insulin therapy.

Keywords: COVID-19, Diabetes mellitus, Hyperglycemia.

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COVID-19 and DM linkage

People who have Diabetes are at increased risk to bacterial and viral infectious diseases, primarily affecting lower airways^{7,8}.

SARS-CoV-2 viruses take over through endocrine pathway to change the mechanism of blood regulation, metabolism and cause inflammation. The receptor of coronavirus, i.e. Angiotensin-converting-enzyme 2 (ACE2) present on the spike protein, which shows a decisive role in the inflammatory cascade⁹.

The S protein(S) of the virus attaches to the host receptors and facilitates the entry of the virus. In a way, the S protein is the entry point for the entry of coronaviruses into target cells. Entry into the host cell depends on the binding of the S protein to a cellular receptor and priming by cellular enzyme proteases. SARS-CoV-2 engages ACE2 as the entry receptor¹⁰. Hyperglycaemia in the pulmonary vasculature at the time of infection has been shown to increase local influenza viral replication in lung tissue¹¹. Current evidence demonstrates that patients with DM are more likely to experience severe symptoms and complications than patients without DM due to COVID-19^{12,13}.

In a study conducted by Bode *et al.* (Glytec Database) on 1122 COVID-19–confirmed patients from 88 US hospitals, the mortality rate was found four-fold higher in diabetic patients (28.8%) as compared to non-diabetic patients (6.2%) and the rate increases with age¹⁴. These findings were supported by a meta-analysis of 33 studies (16,003 patients) conducted by Kumar *et al.* that reported a significant increase in mortality in a diabetic patient with COVID-19 with an odds ratio (OR) of 2.16 as compared to non-diabetics¹⁵.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a viral infectious disease caused by the coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), it was declared a pandemic by the World Health Organization on March 11, 2020¹. Increased morbidity and mortality from COVID-19 in diabetic patients have been observed in countries hardest hit by the pandemic, and this connection, as well as the best management of infected diabetic patients, deserve further investigation. Diabetes is one of the most debilitating and deadly diseases in the world. This is due to the fact that diabetes causes both microvascular and macrovascular complications, both of which can have an effect on diabetic patients' survival rates². Patients with diabetes are highly susceptible to adverse outcomes and complications of COVID-19 infection³. COVID-19 infection causes a disruption in glucose regulation, making glycemic control difficult and necessitating extra caution in diabetic patients⁴. In light of this, it's critical to comprehend the connection between Diabetes Mellitus and Coronavirus disease in 2019. According to ongoing research, patients with diabetes who have poorly regulated glycemia have a four-fold higher mortality risk and a four-fold longer hospital stay than patients without diabetes^{5,6}.



In a retrospective study conducted by Bhandari et al, considered 80 Covid-19 infected patients with T2DM and characterized them with biochemical, radiological and other required clinical parameters¹⁶.

A two-center retrospective study was performed at two tertiary hospitals in Wuhan, China including 1561 patients with COVID-19, representing that a higher proportion of intensive care unit (ICU) admission (17.6% vs. 7.8%, $P=0.01$) and more fatal cases (20.3% vs. 10.5%, $P=0.017$) were identified in COVID-19 patients with diabetes. In addition, the prevalence of diabetes in 27955 Italian patients who died from COVID-19 is 31.1. In the UK, a survey of 23804 patients died from COVID-19 shows the prevalence of T2DM of 32% and T1DM of 1.5%, respectively. In summary, COVID-19 patients with pre-existing diabetes have a worse prognosis, and the mechanisms may be complicated¹⁷.

There is a bidirectional relationship between Covid-19 and diabetes. On the one hand, diabetes is associated with an increased risk of severe Covid-19. On the other hand, new onset diabetes and severe metabolic complications of pre-existing diabetes, including diabetic ketoacidosis and hyperosmolality for which exceptionally high doses of insulin are warranted, have been observed in patients with Covid-19^{18,19,20}.

A retrospective cohort study conducted by Shang et al in Wuhan, analyzed data from 584 patients with COVID-19, including 84 cases of diabetes and 500 cases of nondiabetes. They concluded that diabetes is an independent risk factor for the prognosis of COVID-19²¹.

COVID -19 and DM management

Given the rapid spread of COVID-19 as a result of SARS-CoV-2, there is currently a lot of discussion about how to best treat people with diabetes during this pandemic, including vulnerability to this new infection, the seriousness of the complications, and the function of the drugs to use for glycemic control²². Diabetes, particularly when not well regulated, makes people's lives more difficult and makes them more likely to die^{23,24}.

Patients admitted to the hospital with extreme COVID-19 can need changes to their diabetes care, such as stopping current medications and starting insulin therapy. Such a decision should be based on the severity of COVID-19, nutritional status, actual glycaemic control, risk of hypoglycaemia, renal function, and drug interactions²⁵.

COVID-19 infection exacerbates diabetes mellitus stress by releasing glucocorticoids and catecholamines into the bloodstream. These wreak havoc on glycemic regulation and increase the formation of glycation end products in a variety of organs, both of which worsen prognosis²⁶.

The use of corticosteroids may raise blood glucose by 80% in diabetic patients with COVID-19 infection and to a lesser extent in those without diabetes²⁷.

Blood glucose monitoring is critical in conditions where corticosteroids are needed to maintain near euglycemia and achieve optimal pulmonary and immunologic functions²⁸.

Sardu et al. showed that insulin use achieved better glycemic control in 25 diabetic patients with COVID-19, where the mean glycemia during hospitalization was 10.65 ± 0.84 and 7.69 ± 1.85 mmol/L in non-insulin and insulin-treated groups, respectively ($p < 0.001$)²⁹.

However, metformin has a potential side effect of lactic acidosis, with heightened risk in the context of renal, cardiac and liver impairment, hypotension, and acute illness³⁰. Therefore, current NICE guidance recommends temporary discontinuation of metformin therapy during any acute illness (including COVID-19 infection).

Sulfonylureas can cause hypoglycemia due to low caloric intake during acute infections. It is not ideal in the management of hyperglycemia in COVID-19³¹.

COVID-19 patients with diabetes should have regular glucose monitoring (plasma glucose concentration between 72 and 180 mg/dl) with the estimation of serum electrolytes, pH and blood ketone bodies³².

Patients on insulin therapy should have their blood sugar checked every 2–4 hours, and their insulin dose should be adjusted based on their form of diabetes, comorbidities, and overall health.³³

CONCLUSION

The understanding of COVID-19 interaction is still developing. Anti-diabetic medications that minimise inflammation while maintaining good glycemic control are ideal. Insulin is particularly important in the management of COVID-19 diabetic patients, especially those who have hyperglycemic emergencies or are admitted to the ICU. On going studies suggest that patients with diabetes who have poorly controlled glycemia have around four times higher death rate and longer length of hospitalization compared to patients without DM. Patients admitted to hospital for severe COVID-19 might need modifications to their diabetes therapy, including withdrawing on going treatments and initiating insulin therapy.

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Abbreviations:

DM: Diabetes mellitus

COVID-19: Coronavirus disease 2019

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

ACE2: Angiotensin-converting-enzyme2



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