

## Review Article

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# Coronavirus Disease (COVID-19): 10 Questions and Discussion Points for Diabetes and COVID-19

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## Abstract

The COVID-19 pandemic is now an international concern. COVID-19 is first reported in Wuhan, China on 31 December 2019 and affects different people in different ways. Evidence suggests that people with underlying disease are at higher risk for more severe disease. People with diabetes are not only more likely than the general population to have COVID-19 but also they are among those high-risk categories that can have serious illness if they get the virus.

**Key words:** Clinical Management; COVID-19; Diabetes; Pathogenesis; SARS-CoV-2

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## CONTEXT

The COVID-19 pandemic, also identified as the coronavirus pandemic, caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2), is now suffering the world. 'CO' stands for corona, 'VI' for virus, and 'D' for disease. COVID-19 is first reported in Wuhan, China on 31 December 2019. Coronaviruses (CoVs), enveloped positive-sense Ribonucleic acid (RNA) viruses characterized by a distinctive replication strategy (1). According to the report of the European Centre for Disease Prevention and Control as of 29 March 2020, there have been 4,223,047 reported cases of COVID-19 worldwide, including 291,519 deaths. COVID-19 affects different people in different ways. Most infected people will develop mild to moderate illness and recover without hospitalization. This disease has an incubation period of about 2-14 days and 1-2 weeks of symptomatic disease. In the symptomatic stage, it has a wide variety of symptoms including fever, cough, sore throat, headaches, and in severe form; respiratory problems such as viral pneumonia, respiratory failure, and multi-organ dysfunction (2).

COVID-19 affects all age groups. However, evidences to date suggest that two groups of people are at higher risk of developing more severe disease, including older adults (i.e. people over 60 years old); and people with underlying diseases

such as cardiovascular diseases, diabetes, chronic pulmonary disease, and malignancy (3). More than 425 million people worldwide have diabetes. People with diabetes are not only more likely than the general population to have COVID-19 but also they are amongst those high-risk categories that can have serious illness if affected by virus (4). However, nowadays a dearth of data still exists on the management of diabetes during the COVID-19 pandemic.

## EVIDENCE ACQUISITION

The main keywords, i.e. COVID-19, coronavirus, SARS-CoV-2, diabetes and, clinical presentation of COVID-19 were used to search in the scientific databases. The authors reviewed the literatures published, using Medline, Scopus, Cochrane database for systematic reviews and Scopus, Web of Science, PubMed, and Google scholar search engines. All types of articles, such as reviews, originals, letters, and etc., were included in the study. The most relevant articles were studied and summarized. Finally, the best articles related to the context of the subject were selected and required information were extracted.

## RESULTS

For better understanding the findings were

categorized and discussed in reply to 10 questions, based on current knowledge

## DISCUSSION

### 1) *Are people with diabetes at increased risk to get COVID-19?*

Individuals with diabetes are at risk of infections (5). But based on current knowledge people with diabetes are not only more prone to have COVID-19 than the other people but also they are more susceptible to get more severe disease. They are at an increased risk of getting acute respiratory distress syndrome (ARDS) and increased mortality. Also, the symptoms and complications of COVID-19 are more common in people with diabetes than in the general population (6).

### 2) *What are the factors associated with the severity of covid19 in subject with diabetes?*

In certain cases, patients with diabetes are at higher risk to get serious complications from COVID-19. For example, they are at increased risk of getting very sick if their blood sugar is not controlled (7). Aging, history of cardiovascular disease, chronic lung and kidney disease, and hypertension are associated with a higher chance of COVID-19 severity. Beside them; ethnicity, body mass index, and some medication can play a role in the severity of COVID-19. Therefore special attention should be paid to underlying diseases in patients with diabetes, especially among the elderly (8). Among biochemical biomarkers, the presence of lymphopenia and an increase in interleukin 6 and CRP are associated with severe disease (8).

### 3) *Are the chances of developing COVID-19 different in type 1 and type 2 diabetes?*

There is not enough evidence to differentiate between the risk of COVID-19 and types of diabetes. But we do know that these two types of diabetes are different in terms of age, the onset of complications, and treatment options. Therefore, people with diabetes (regardless of diabetes type) should take the necessary precautions to prevent COVID-19 (8).

### 4) *What is the reason for worsening the outcome of covid 19 disease in patients with diabetes?*

COVID-19 in diabetic subject probably create higher stress situations, with the greater secretion of counter-regulatory hormones, it can trigger to high blood glucose level and fluctuation in the blood glucose. The reasons for the worsened outcomes for those with hyperglycemia aren't understood. Beside, Hypoglycemia increases cardiovascular mortality in people with diabetes

possibly by mobilizing pro-inflammatory monocytes and increasing platelet reactivity (8). Now, we don't have enough information about the occurrence of inflammatory and immune responses in patients with diabetes, furthermore, there is little evidence for changing the virulence of the COVID-19 by hyper or hypoglycemia or effects of the virus on insulin secretion or glycemic control. Various mechanisms have been proposed to increase the susceptibility of patient with diabetes to more severe COVID-19. Diabetes is an inflammatory disease that causes the production of advanced glycation End-products (AGEs) and inflammatory factors by increasing the glycosylation. Uncontrolled diabetes is also associated with inhibition of lymphocyte proliferation and neutrophil dysfunction. Angiotensin 2 converter enzyme is one of the main receptors for SARS-CoV (8). This enzyme acts as a receptor for the virus to enter the host lung pneumocyte cells and causes lung damage (9). Pancreatic cells are one of the receptor sites; SARS-CoV can damage the pancreas and eventually make the disease worse. Reduction in viral clearance and insulin resistance are other mechanisms involved in the disease severity in diabetic patients (7). This inflammatory response possibly could explain differences in susceptibility to more severe infections with worse consequences in diabetes.

### 5) *What preventative measures can patient with diabetes take against the coronavirus disease?*

Based on our current understanding people with diabetes are at high risk for developing more severe COVID-19 especially when they have an underlying condition. The first point is that if a person with type-2 diabetes finds any signs of COVID-19 symptoms, they should consult with their doctor about their medication. Secondly, like everyone else in the community, diabetics need to take the necessary precautions to prevent COVID-19. In particular, to prevent COVID-19 in a patient with diabetes, it is recommended to control their glycemic, performing more physical activity and, have accurate monitoring of blood sugar to reduce the risk of complications from COVID-19 (10).

### 6) *Is it necessary to change the treatment of diabetic patients if hydroxychloroquine is started?*

Hydroxychloroquine is one of the drugs used in COVID-19 (11). It can reduce insulin post receptor clearance, facilitate glucose transfer by insulin and, suppress inflammatory biomarkers (12). Therefore, it can cause hypoglycemia and required dose adjustment in diabetic patients especially if

they have increased risk for hypoglycemia. The safely uses of hydroxychloroquine in diabetic patients with COVID-19 improve blood sugar, decreased requirements insulin, and decreased HbA1c levels (11).

**7) Are people with diabetes more prone to DKA if they get COVID-19?**

Like other viral infections, diabetics with COVID-19 are prone to ketoacidosis commonly experienced by people with type-1 diabetes (13). Diabetic ketoacidosis (DKA) can complicate fluid and electrolyte management which is important in managing infection.

**8) How is the management of diabetic patients with COVID-19 infection in outpatient setting?**

Healthcare workers should sensitize the subjects with diabetes for the importance of optimal metabolic control and current diabetic treatment. They don't discontinue their treatment without physician advice. It is important to know there is no need to prophylactically discontinue diabetic treatment for out-patients COVID-19 with diabetes. For better care of diabetes patients using virtual care is recommended (14).

**9) How is the management of diabetic patients with COVID-19 infection in inpatient setting?**

First, every patient hospitalized with a COVID-19 infection needs to be screened for new onset diabetes. Afterward, its necessary to optimize glycemic control in an attempt to reduce the risk of severe COVID-19 disease. In the case of severe COVID-19 disease, insulin therapy should be started. It is important to check the potassium balance carefully following the initiation of insulin. Because hypokalemia is common in COVID-19 (possibly due to association with hyperaldosteronism induced by high concentrations of angiotensin-2) and it can be exacerbated if insulin is started (13).

**10) Should oral hypoglycemic agent in diabetics be changed in the event of a COVID-19 infection?**

Careful glycemic control is necessary to lessen the

risk of severe COVID-19 disease. The general rule for treating diabetic patients in the context of COVID-19 is that there is no need to change medication if they have a mild illness and are treated on an outpatient basis. In diabetic patients with severe symptoms of COVID-19, treatment with metformin and sodium-glucose co-transporter-2 (SGLT2) inhibitors should be discontinued due to the possibility of lactic acidosis and euglycaemic ketoacidosis respectively. Basically, if oral medication is stopped, the alternative treatment would be insulin therapy (15).

**CONCLUSIONS**

COVID-19 has been rapidly expanding since its inception in Wuhan. Diabetes is one of the risk factors for the increased severity and augmented mortality in patients with COVID-19. Timely diagnosis and proper management of the disease in people with diabetes is associated with a better control. The association between diabetes and COVID-19 is largely unknown. Our information about COVID-19 is increasing day by day. Recent data is mostly based on both assumption and factual. However, these data provide a basis for future research on the pathophysiological mechanism of COVID-19 in patients with diabetes.

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**AUTHORS' CONTRIBUTION**

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**CONFLICT OF INTEREST**

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