

## Glucovigilance in COVID-19

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### Abstract

The coronavirus disease (COVID-19) pandemic has influenced clinical care in unprecedented ways. There is an urgent need to share best practice in providing diabetes care services in areas affected by COVID. This is a brief review for clinicians managing diabetes in low-income countries based on currently available data. The data is rapidly evolving; however, people with diabetes and its related comorbidities have increased risk for severe disease, and prolonged recovery and mortality. This review is also informed by data from severe acute respiratory syndrome (SARS) caused by SARS coronavirus (SARS-CoV) and Middle East respiratory syndrome (MERS), caused by MERS coronavirus (MERS-CoV). These two viruses share similarities with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus with causes COVID-19. SARS-CoV-2 was also known as 2019-nCoV. We discuss glucovigilance in COVID-19, the challenges and the opportunities. We put a spotlight on investigational new drugs for treatment of COVID medications and virtual care. Diabetologists and clinicians handling high-volume diabetes clinics are at increased risk for contracting COVID-19.

**Keywords:** COVID-19, Glucovigilance, Prognosis, Diabetologists, Social distancing, Type 1 diabetes, Type 2 diabetes.

**DOI:** <https://doi.org/10.5455/JPMA.15>

### Introduction

The current coronavirus pandemic was first detected in Wuhan, Hubei, China in January 2020. The virus (severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) has since claimed 100,000 lives with over 2,000,000 infections globally. Coronavirus disease (COVID-19) shares similar symptomatology with SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), which

caused epidemics in 2002 and 2012 respectively. The 2002 SARS-CoV affected 8,422 people and caused 916 deaths. The MERS-CoV affected 1,600 people with 574 deaths. MERS-CoV has not yet been contained with 249 confirmed cases and 858 deaths. Commonly, COVID-19 is associated with malaise, fever, dry cough, anorexia, dyspnoea, lymphopenia and disordered bleeding.<sup>1-3</sup> Persons with diabetes seem to be at increased risk for severe disease and mortality from COVID.<sup>3-10</sup> This paper discusses COVID-19 and diabetes care in low resource settings.

### Background

COVID-19 is caused by the SARS-CoV-2 virus, a beta-coronavirus. It is a zoonotic disease similar to SARS and MERS. These viruses cause acute lower respiratory disease with poor clinical outcomes in the elderly and those with comorbidities. Currently treatment is supportive as there are no effective anti-viral agents.<sup>3,4</sup>

### Diabetes and COVID-19

#### Pathophysiology

The virus enters cells via angiotensin converting enzyme 2 (ACE2) receptor which are abundant in the lungs and the pancreas.<sup>4,6</sup> Binding of the s-glycoprotein from SARS-CoV-2 to ACE-2 results in internalisation of the virus. This triggers an inflammatory response with the recruitment of T-helper cells that produce interferons. The course of the disease depends on the degree of the immune response. In severe disease, the immune system goes into overdrive resulting in a "cytokine storm". This is responsible for multi-organ failure seen in severe disease.

Poorly controlled diabetes is known to interfere with humoral immunity. Additionally, the following factors increase susceptibility for severe COVID disease in diabetes:

- ◆ increased expression of ACE2 receptors
- ◆ inability to suppress viral replication due to altered T-lymphocyte response
- ◆ influx of cytokines particularly interleukin

Studies from Wuhan show that people with diabetes take longer to clear the virus compared to those

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without diabetes.<sup>5</sup>

### **Diabetes: A Risk Factor for COVID-19**

The Chinese Center for Disease Control and Prevention (CDC) classifies COVID as mild, moderate or severe based on clinic-pathological features. In mild disease, pneumonia is absent or if present is mild. Moderate disease is defined by pneumonia with dyspnoea, respiratory rate >30 breaths per minutes and oxygen saturation below 93%, or presence of mild pneumonia. Severe disease is characterised by respiratory failure, septicaemia and multi-organ damage.<sup>4</sup>

Several studies have identified chronic cardio-vascular conditions as pre-disposing factors for SARS-CoV-2 infections. Diabetes is associated with an increased risk for severe disease, admission to critical care units and mortality.<sup>4,7</sup>

### **Glucovigilance in Pharmacotherapy of COVID-19**

Agents used in the management of COVID-19 can interfere with carbohydrate metabolism thus it is important to be pro-active when managing patients. Glucovigilance, must be heightened necessarily and the threshold for insulin initiation and intensification reduced. More frequent testing despite the associated costs must be prioritised.

### **Hydroxychloroquine/Chloroquine and COVID-19**

Hydroxychloroquine causes non-insulin related hypoglycaemia and prolongation of the QT interval. Its use is associated with cardio-vascular, cerebrovascular, neurologic and ophthalmic complications. Hydroxychloroquine is associated with the 'dead-in-bed syndrome', cognitive and language defects, myocardial infarcts, cerebrovascular accidents, aggravation of proliferative retinopathy and retinal haemorrhages.

### **Corticosteroids**

The use of corticosteroids though controversial is very common in ICU settings.<sup>9</sup> Corticosteroids are counter regulatory to the action of insulin. Steroids inhibit hepatic gluconeogenesis, peripheral glucose uptake and glycogenesis by skeletal muscles, decrease pancreatic insulin production and increase lipolysis in adipose tissues. These cumulatively result in hyperglycaemia, particularly in people with dysglycaemia or pre-existing diabetes. A meta-analysis conducted by Zhenwei Yang and Jialong Liu pooling together 5270 patients with coronavirus pneumonia (from 2002 to March 15, 2020)

concluded that corticosteroid therapy is not only associated with hyperglycaemia (RR = 1.37, 95% CI = 0.68-2.76, p=0.376) but also with high mortality (RR = 2.11, 95% CI = 1.13-3.94, p=0.019).<sup>9</sup> Glucose control and monitoring must be enhanced with the use of corticosteroids. Glucovigilance is key in such settings.

### **Antiviral agents**

Protease inhibitors (lopinavir/ritonavir) interfere with glucose metabolism particularly in the settings of diabetes and or obesity.<sup>10</sup> This effect is dependent on the duration of use.

### **Long-term Complications of COVID on Cardio-Metabolic Health**

There is no data on long-term outcomes of COVID-19. A 12-year follow up of survivors of coronavirus infections showed high prevalence of cardio-metabolic disorders. Prevalence of dyslipidaemia, dysglycaemia and cardiac disorders were 68%, 60% and 44% respectively.<sup>11</sup> Insulin resistance, hyperinsulinism, hyperglycaemia and diabetes were also noted among the cohort.

### **COVID-19 and Diabetes Services**

Globally, COVID-19 has disrupted not only health but health systems as well. The impact on health systems is more devastating in low-income countries where access to virtual systems/services is limited or unavailable.

Public health interventions such as lockdown and social distancing have resulted in loss of income, further reducing access to daily necessities, medications and non-urgent clinical services. Patients who live in "medically underserved" areas and those without health insurance coverage have been hit the hardest.

Inadequate PPEs leave healthcare workers in low-income settings at increased risk for becoming infected. It also increases the likelihood of hospitals becoming epicentres for secondary infection. Lack of guidelines on management of diabetes in COVID-19 hampers care.

### **COVID-19 - An Occupational Risk for Diabetologists**

COVID-19 is an occupational hazard for all health workers. The risk is heightened for diabetologists and diabetes services with high volume. Infections among health workers have grave short and long-term implications for service delivery, training and research. For low-income countries with weak health care systems, low provider-to-patient ratios, and a double burden of disease the COVID-19 epidemic can be likened to a tsunami.

## Conclusion

The data is still evolving but diabetes seems to be associated with more severe forms of COVID-19 and prolonged recovery. Medications used in the management of COVID may interfere with carbohydrate metabolism. This necessitates increased glucovigilance during care. Although the use of virtual services reduces risk of transmission to and among healthcare workers, these options remain largely unavailable in low-income countries. The repercussions of this pandemic are far reaching beyond health systems and a slow long recovery lies ahead.

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