

# Care for diabetes with COVID-19: Advice from China

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The epidemic of the coronavirus disease 2019 (COVID-19) has expanded from Wuhan throughout China and is being exported to a growing number of countries outside of China.<sup>1</sup> The growing epidemic of COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>2</sup> The potential public health threat posed by COVID-19 is very high, both to China and globally. By 9 March 2020, 80 904 cases of COVID-19, including more than 3123 deaths, had been confirmed in China, mainly in Hubei province.<sup>3</sup> A further 28 673 laboratory confirmed cases have been reported across 104 other countries/territories/areas.<sup>3</sup> Considering the high proportion of critically ill patients with diabetes or hyperglycemia, the difficulty for treatment and high mortality rate, effective diabetes management under epidemic conditions is extremely important. In order to increase disease awareness and improve the prognosis and outcome of patients with diabetes, better understanding of the etiological associations between COVID-19 and diabetes, the clinical impact of COVID-19 on diabetes, and proposing detailed recommendations for prevention and treatment are needed.<sup>4,5</sup>

## 1 | ASSOCIATIONS BETWEEN COVID-19 AND DIABETES

Epidemiologic evidences suggest that diabetes is associated with high risk of infectious diseases. People with diabetes are at increased risk for the bacteremic form of pneumococcal infection and have been reported to have

a high risk of nosocomial bacteremia, with a mortality rate as high as 50%.<sup>6</sup> In the nationwide China Cardiometabolic and Cancer Cohort (4C) study, compared to those with normal glucose tolerance, individuals with impaired glucose tolerance or diabetes had 50-60% higher risk of pulmonary infection. In this epidemic of COVID-19, the affected population had higher prevalence of diabetes, especially in critically ill patients. The first study published on 41 cases of COVID-19-infected people in Wuhan reported that in 32% of cases COVID-19 was combined with other diseases, including diabetes (20%), hypertension (15%), and cardiovascular disease (CVD; 15%).<sup>7</sup> Subsequently, another study of a total of 99 infected persons showed that 52% of the infected persons had increased glucose levels.<sup>8</sup> A retrospective study of 138 patients with COVID-19 published on 7 February 2020 showed that 64 (46.4%) had one or more underlying diseases, of which 10% (14/138) had diabetes, whereas in intensive care units (ICU), 22.2% (8/36) patients had diabetes.<sup>9</sup>

Metabolic disorders further influence the severity of COVID-19. It is noted that, compared to subjects with no comorbidities, severe pandemic influenza cases are significantly elevated with obesity (OR for mortality 2.74, 95% CI, 1.56-4.80).<sup>10</sup> Similar findings were reported in other respiratory illnesses such as Middle East respiratory syndrome coronavirus (MERS-CoV) and swine influenza (H1N1). From current clinical reports, COVID-19-affected patients with diabetes are at high risk of becoming critically ill and of death. The findings from Wuhan Jin Yin Tan Hospital demonstrated that in ICU,

17% patients were reported to have chronic medical illnesses, including diabetes (17%), cerebrovascular diseases (13.5%), chronic cardiac diseases (10%), etc. During ICU treatment, 35% patients were reported to have hyperglycemia as comorbidity. More strikingly, the mortality in diabetics was as high as 77.7% (7/9) among critically ill patients. Evaluating the prevalence of these chronic conditions is fundamental to mitigate COVID-19 complications.<sup>11,12</sup> Early identification of individuals who are at risk of becoming critically ill and who are most likely to benefit from ICU is of considerable value.

Metabolic syndrome-related conditions such as diabetes, hypertension, CVD, and obesity together with their predisposing conditions can be etiologically linked to COVID-19 pathogenesis. During infection, the coronavirus may destroy islets through its functional receptor angiotensin-converting enzyme 2 (ACE2) in islets and make diabetes progress. The SARS-CoV-2 virus can also effectively use ACE2 to enter cells to infect humans.<sup>2</sup> No direct evidence was identified genetically supporting the existence of coronavirus S-protein binding-resistant ACE2 mutants in different populations.<sup>13</sup> Dysglycemia is known to downregulate key mediators of host innate immune response to pathogenesis. In patients with diabetes, hyperglycemia and insulinopenia attenuate the synthesis of pro-inflammatory cytokines and their downstream acute phase reactant to functionally impair the innate and humoral immune systems of the host. Furthermore, metabolic disorders reduce immune response by impairing macrophage and lymphocyte functions,<sup>14</sup> which might subsequently render individuals more susceptible to infectious disease complications.

## 2 | SPECIAL CONSIDERATIONS FOR PATIENTS WITH DIABETES DURING THE EPIDEMIC

During the outbreak of COVID-19, we recommend the “Seven Treasures” policy for diabetes management, including health education, balanced nutrition, physical activity, standardized medication, blood glucose monitoring, regular schedule, and care for mental health. “Five No” (no going out, no gatherings, no sedentariness, no stop on medications, no anxiety), “Five Keep” (keep wearing a face mask when you go out, keep hands clean, keep routine medical check if necessary, keep regular life, keep scientific attitude to COVID-19), and “Five Refuse” (refuse to visit friends, refuse group dining, refuse to taste wild animals, refuse rumors, refuse to shake hands or hug or kiss) should be advocated for patients with diabetes by endocrinologists, healthcare providers, and public health administrators.

For metabolically stable patients, a monitoring frequency for fasting and postprandial glucose levels of two to three times per week is acceptable. If marked hyperglycemia is indicated (blood glucose consistently exceeds 13.9 mmol/L) or severe symptoms (eg, thirst, dizziness, fatigue, nausea) occurred, timely hospital management is required. Two-way referral system should be established between the general practitioners and endocrinologists, and the specialists should provide training and guidance to the general practitioner during the epidemic.

## 3 | GLYCEMIC MANAGEMENT FOR COVID-19-AFFECTED DIABETES PATIENTS

Healthcare personnel are on the front line of caring for patients with confirmed or possible infection with COVID-19. Personal protective equipment, routine cleaning, and disinfection procedures are appropriate for SARS-CoV-2 in healthcare settings, including those patient care areas in which aerosol-generating procedures are performed. Management of laundry, food service utensils, and medical waste should also be performed in accordance with routine procedures. The examination of eye diseases can be postponed due to the potential risk of COVID-19 infection through the conjunctiva, if not urgent.

### 3.1 | Individualized glycemic recommendation

Individualized goals for blood glucose control should be recommended in the treatment. For nonsenile patients with mild or ordinary type of COVID-19, glucose targets are as follows: fasting blood glucose 4.4 ~ 6.1 mmol/L, 2-hour postprandial or random blood glucose 6.1 ~ 7.8 mmol/L. For older patients with mild or ordinary type of COVID-19 or in use of glucocorticoid, the goals are less stringent: fasting blood glucose 6.1~7.8 mmol/L, 2-hour postprandial or random blood glucose 7.8~10.0 mmol/L. In severe or critically ill cases of COVID-19, a fasting blood glucose of 7.8~10.0 mmol/L and a 2-hour postprandial or random blood glucose of 7.8~13.9 mmol/L should be achieved.

### 3.2 | Pharmacological therapy for diabetes

A patient-centered approach should be used to guide the choice of pharmacologic agents. Considerations include

age, severity of COVID-19, cardiovascular comorbidities, and hypoglycemia risk. For patients with mild COVID-19, previous medication regimens should be evaluated and followed as appropriate. For ordinary cases, subcutaneous insulin injections, including rapid-acting prandial/basal insulin or premixed insulin regimens, are recommended. For severe and critically ill patients, intravenous insulin therapy may be the preferred treatment.

The past two months have seen tremendous efforts of medical staff to address the condition of critically ill patients and safeguard the public health in China. With the epidemic under control, people are gradually coming back to work, and clinics are back in service to the public. We are now at a critical stage of the prevention and control of the COVID-19 epidemic. Endocrinologists should understand the impact of the epidemic on diabetic patients. It is important to follow standard hospital management and treatment regimens for COVID-19-affected patients with diabetes. Meanwhile, we should pay attention to the lifestyle and glucose management of patients with diabetes outside the hospital and provide them precise medical services. We also suggest that, if possible, global cooperation is needed in medical research, to better understand the genetic, molecular, and immune mechanisms explaining the interplay between COVID-19 and diabetes, and the interplay between disease features, such as susceptibility, severity, and outcome of diabetic patients, with COVID-19 in different populations. We believe, all our efforts will finally overcome COVID-19.

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#### CONFLICT OF INTEREST

None declared.

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