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COMMENTARY

Diabetes and the COVID-19 Pandemic: How Insights from Recent Experience Might Guide Future Management

Anca Pantea Stoian, MD, PhD,[1] Yajnavalka Banerjee, MD, PhD,[2] Ali A. Rizvi, MD, PhD,[3] and Manfredi Rizzo, MD, PhD[4,5]

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COVID-19 is an acronym formed by ''CO'' for corona, ''VI'' for virus, and ''D'' for disease. The ''19'' represents 2019—the year when the infection started. This new disease was unknown before the outbreak began in China in the city of Wuhan, and now it is a serious health problem worldwide.[1] Indeed, COVID-19 is a rapidly spreading communicable disease, and its severity has varied from mild self-limiting flu-like illness to fulminant pneumonia, respiratory failure, and death.[2] Older people and those with chronic diseases, including diabetes, are more likely to develop more severe symptoms and complications. Therefore, in order to limit the spread of the disease, millions of people have now been forced indoors and into isolation or quarantine. Yang et al. recently published a small but very informative systematic review and meta-analysis on the prevalence of comorbidities associated with COVID-19 infection in China, and they reported that diabetes was prevalent in 8% of cases, highlighting that this is somewhat in line with the prevalence of diabetes (10.9%) in Chinese adults.[3]

Yet, from the reports made so far on this infection in different countries, it seems that the presence of diabetes is linked to greater mortality and also a greater need of intensive care during COVID-19 infection. In a retrospective cohort study, Zhou et al. reported on the clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China. The authors included all adult inpatients ($N = 191$) with laboratory-confirmed COVID-19 from two hospitals in Wuhan, and they found that diabetes was the second most common comorbidity after hypertension. Indeed, the prevalence of diabetes was 19% in the total cohort of patients and differed significantly when patients were stratified by outcome: those who survived (14%) versus those who died (31%).[4] However, the mechanisms driving this difference in outcome have so far not been elucidated.

It is generally known that patients with diabetes mellitus, especially those with type 2 diabetes (T2DM), are more susceptible to infections, including those of the respiratory tract. In adult patients, COVID-19 seems to manifest in the most severe forms in those with diabetes and other comorbidities, such as high blood pressure, cardiovascular disease, and obesity. Patients with T2DM usually present with excess adipose tissue, which enhances chronic inflammatory and prooxidative states that have a negative impact on glycemic profile, thus deteriorating both glycemic homeostasis and peripheral insulin sensitivity.[5] Thus, the chronic hyperglycemic state and chronic inflammatory state are the two pathophysiologic elements of immunosuppression that take place in T2DM patients at higher risk of COVID-19 infection, and also represent an increased risk of mortality *per se*.[2] It is still unknown if the chronic imbalance of diabetes mellitus—namely, the chronic hyperglycemic state—contributes to the virulence of COVID-19 expression and if this can lead to major changes in the metabolism of carbohydrates in T2DM patients.[6]

Although the data regarding diabetes management during COVID-19 are still scarce and the profiles of diabetic patients more susceptible to the infection are not precisely known, it is, however, notable that in the study conducted in Wuhan, China, 31% of COVID-19 patients who died had diabetes.[4] This finding is very consistent with recent data from Italy, where the number of patients infected followed an exponential trend.[7] A recent analysis of 909 deceased COVID-19 patients in Italy showed that diabetes was the second most common comorbidity (31.5%) after hypertension (73.5%).[8] Regarding other European countries, on March 27 in Spain,

[1]Diabetes, Nutrition and Metabolic Diseases, University of Bucharest, Bucharest, Romania.
[2]Department of Biochemistry, Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai, United Arab Emirates.
[3]Division of Endocrinology, Metabolism, and Lipids, Department of Medicine, Emory University, Atlanta, Georgia, USA.
[4]Department of Medicine, University of South Carolina, Columbia, South Carolina, USA.
[5]Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, University of Palermo, Palermo, Italy.

5,466 deaths were declared, and the prevalence of diabetes was 12%.[9] In Romania, out of the 69 patients who had died by the end of March, more than half suffered from cardiovascular diseases and diabetes mellitus.[10]

On the basis of the above data, the clinical evolution of patients with diabetes and COVID-19 can be severe and even fatal in older ages and when suffering from comorbidities including cardiovascular, pulmonary, kidney, and renal diseases. In such situations, diabetes management can be challenging, and special attention should therefore be paid to this cluster of patients. Some general recommendations for patients with diabetes and COVID-19 have been recently formulated by different scientific societies such as the American Diabetes Association, including[11]: drinking lots of fluids to avoid dehydration; maintaining glycemic balance close to the individualized target values; monitoring blood sugar levels at extra times throughout the day and night in order to avoid hypoglycemic episodes and ketoacidosis; and preserving rigorous hygiene, such as washing hands and cleaning the injection/infusion and finger-stick sites with soap and water or rubbing alcohol.

The treatment of comorbidities, especially coexisting high blood pressure, dyslipidemia, or cardiovascular or renal diseases, must not be interrupted. In the case of COVID-19, an important element is the molecule that has the role of receptor for the virus: the angiotensin-converting enzyme 2 (ACE2), which is found at the surface of the cells that pad the respiratory airways and the lungs, thus facilitating the virus entering the body.[12] At the same time, ACE2 is a target of the antihypertensive therapeutic class named angiotensin-converting-enzyme inhibitors. Taking into account the high prevalence of hypertension among the severe cases of COVID-19, different hypotheses have been formulated, suggesting that hypertensive patients taking such medications are at a high risk of infection with COVID-19 because of the high level of the enzyme at whose level the virus is bound.[12] However, the European Society of Cardiology recommends that patients and doctors should continue the usual antihypertensive treatment because there are is so far no clinical data or scientific evidence suggesting that ACE inhibitor medications should be interrupted because of infection with COVID-19.[13] On the other hand, incretin-based therapies may be beneficial in T2DM patients and COVID-19, besides their beneficial effects on glucose metabolism.[6]

In the meantime, as more data about COVID-19 become available, we wish to emphasize the optimization of physician–patient communication for diabetes management in the era of social distancing, isolation, and quarantine. Even though the presence of diabetes increases the risk of adverse outcomes related to morbidity and mortality in the event of COVID-19, this situation may have a silver lining. As long as patients have mild to moderate symptoms that can be managed at home and they have nominal expertise and access to technology, the lines of communication between affected diabetic patients and their care providers can be maintained quite unobstructed.[14] This can be done without the need for physical office visits.

In this respect, there may be several ways for patients to reach out to their diabetes specialists:

(1) In the era of the electronic medical record (EMR), most patients are able to message their physicians directly with questions and concerns. For example, the majority of EMR systems offer patients the option of signing up with a ''portal'' that links to their email address in a privacy-compliant and confidential manner.[15] They can also send their glucose readings, either by typing them in or attaching downloads from their traditional blood glucose meter, or by using continuous glucose monitoring (CGM) techniques. Of note, several CGM device makers offer the creation of personal accounts for patients and password-protected platforms for physician practices to interface with patients' CGM gadgets and insulin pumps.[16] Such means of interaction also gain added importance and usefulness for physicians to keep in touch with patients and allay their fears and anxieties.

(2) As long as physician offices and health-care systems keep phone triage and call center access in place, the old-fashioned telephone is still available and preferred by many older patients who might be ''technology challenged.'' An automated mechanism or answering service that routes messages to an on-call doctor or allied health professional can be vital in this regard.

(3) Where video teleconferencing resources are available, clinic visits may be replaced by telemedicine encounters with face-to-face audiovisual interaction. Such instances provide a similar level of patient and provider satisfaction as actual visits,[17] with physical examination lending itself to general appearance and inspection as well. These visits are billable, are rapidly become the default mode of medical visits for urgent reasons, and may become the way routine visits are conducted if the pandemic continues for a long duration.[18] Patients with diabetes stand to benefit from televisits, since interviewing and inspection predominate rather than palpation and auscultation.

In summary, the COVID-19 pandemic is a huge challenge for diabetic patients and diabetologists, but it can be also an opportunity to improve physician–patient communication for better management of the disease in the era of social distancing, isolation, and quarantine. Diabetic patients need special attention and care, since it seems that their disease is associated with increased severity of symptoms and complications with COVID-19.

Author Disclosure Statement

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Address correspondence to:
Assoc. Prof. Anca Pantea Stoian, MD, PhD
Diabetes, Nutrition and Metabolic Diseases Department
University of Medicine and Pharmacy Carol Davila
8 Eroii Sanitari Str, 050474
Bucharest
Romania

E-mail: ancastoian@yahoo.com