



# Covid-19 and diabetes: when a pandemic cross another pandemic

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## Abstract

The Covid-19 epidemic is having a strong impact on the population with pre-existing chronic diseases. The collision between the Covid-19 pandemic and the current diabetes epidemic has highlighted that obese and diabetic patients have a worse prognosis due to the impairment of the immune response to infections and due to the mechanical limits that make the management of the hospitalized patients with severe obesity more difficult. The limitations imposed on accessibility to non-urgent care during the lockdown of "phase 1" of this pandemic have created the need to revolutionize clinical practice to meet the health demands of chronic and high-risk diseases such as obesity and diabetes. The use of technology and risk stratification to establish the priority of access to the treatments that we have been forced to undertake will be useful tools for a new phase of a more efficient and successful treatment of diabetes.

Coronavirus disease-2019 (COVID-19), caused by the new corona virus SARS-CoV-2, is a pandemic that originated in China in December 2019, spread worldwide in a few months. As May 14, 2020, there are over 4 million cases of contagion worldwide and over 290.000 deaths. The United States rank first with over 1 million infections and over 84.000 deaths. Italy is in third place for deaths (over 31.000) and in fifth place, after Spain, for infections (over 220.000) [1].

"Diabetes" was considered the pandemic of the 3rd millennium until Covid-19 outbreak. The term underlines the intricate relationship between obesity and type 2 diabetes (T2DM). Most patients with T2DM are affected by obesity and the global rise in obesity largely explains the epidemic rise in incidence and prevalence of T2DM over the last few decades [2].

The use of the term "diabetes" and the attempt to consider obesity and diabetes as a single disease and not as two separate entities seems to be particularly important in the context of the COVID-19 pandemic.

The "Diabetes" epidemic is likely to be the biggest epidemic in human history up to February 2020 when WHO declared Covid-19 pandemic [3].

The Covid-19 outbreak clinical picture is variable: the more severe cases are characterized by the development of a severe acute respiratory syndrome caused by extensive pulmonary fibrosis which is responsible for the high mortality in Italy (31.106 total deaths as May 14). In 31.5% of the reported cases at least one co-morbidity is reported (cardiovascular, respiratory, diabetes, immune deficiencies, metabolic, oncological, obesity, renal or other chronic disorders) [4].

Data from the Intensive Care National Audit & Research Centre (ICNARC) report on COVID-19 in critical care of United Kingdom (March 27th 2020) described that 72.1% of 775 patients with confirmed COVID-19 were overweight or obese and that among patients with Body Mass Index (BMI) > 30 kg/m<sup>2</sup> who had undergone intensive care, 60.9% of them died.

Extensive Chinese observational reports on confirmed Covid-19 cases indicated that among patients with the most severe form of disease the prevalence of diabetes was 12–16% [5–8].

In Italy, as regards COVID-19 pandemic, the data reported by the ISS (Istituto Superiore di Sanità), updated to 7 May, obtained from 2621 death, report that obesity was present in 11% of cases and diabetes in 31.1% of cases [4].

As regards our experience at the S.M. Goretti Hospital in Latina, from 6 March to 14 April 2020, among 89 hospitalized patients with an average age of 58 years (55.1% male), 18% had a BMI ≥ 30 kg/m<sup>2</sup>, 10.1% had a known diabetes and 20% (known and newly diagnosed diabetics) required insulin

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therapy for glycemic rise secondary to steroid treatment. Moreover, 5.6% of our patients was affected by diabetes and almost 28% of patients with diabetes was affected by obesity, but the data are continuously updated.

Based on literature data, diabetes may not increase the risk of SARS-CoV-2 infection but can worsen the outcome [9]. In patients with obesity and diabetes, the expression of ACE2, the functional receptor for SARS-CoV, is upregulated in adipocytes and turns adipose tissue into a potential target and viral reservoir. This may explain why obesity and diabetes are potential empowering factors for COVID-19 infection [10].

A summary report from the Chinese Center for Disease Control of 72,314 cases across the country showed a higher mortality rate in people with diabetes, compared to non-diabetics, which further proves that diabetes is a risk factor for the prognosis of COVID-19 [11].

Moreover, obesity is an independent risk for hypoventilation syndrome in Intensive Care Unit (ICU) patients [12] and so could contribute to respiratory failure in patients with acute respiratory distress syndrome (ARDS) [13].

In a French study, the risk for invasive mechanical ventilation in patients with COVID-19 infection admitted to Intensive Treatment Unit was more than sevenfold higher for those with BMI > 35 compared with BMI < 25 kg/m<sup>2</sup> [14]. Among individuals with COVID-19 aged less than 60 years in New York City, those with a BMI between 30–34 kg/m<sup>2</sup> and > 35 kg/m<sup>2</sup> were 1.8 times and 3.6 times more likely to be admitted to critical care, respectively, than individuals with a BMI < 30 kg/m<sup>2</sup> [15].

In addition to the evident difficulty of treatment for patients with extreme obesity (e.g., BMI > 40 kg/m<sup>2</sup>), due to difficult intubation, extubation, insertion of central IV-line, appearance of pressure ulcers, size limitations of diagnostic capabilities (MRI), lack of extralarge beds to accommodate this patients in medical units/ICUs, Sattar et al. from University of Glasgow speculated that one of the pathways by which obesity (and/or excess ectopic fat) may increase the severity of COVID-19 infection is the amplified or dysregulated immune response typical of the patient with obesity, that could mediate the progression to critical illness and organ failure [16].

It should be also emphasized that in patients with obesity the response to antiviral and antimicrobials drugs is poorer, the response to vaccine is reduced [17] and the adaptive immune responses to influenza virus is impaired [18] such as in patients with diabetes [19].

Therapies taken by patients with diabetes could also have an impact on Covid-19 infection, in fact insulin administration attenuates ACE2 expression [20, 21], while glucagon-like peptide-1 (GLP-1) agonists (liraglutide) and thiazolidinediones (pioglitazone), antihypertensives such as ACE inhibitors, and statins upregulate ACE2 [22–24].

In consideration of clinical experience and literature data, the presence of diabetes can be a further alarm in the management of Covid patient which should guide clinicians in the timing of the start of drug therapy and hospitalization.

On the other hand, the limitations imposed on accessibility to non-urgent care during the lockdown (phase 1) have postponed the outpatients' clinic access, favoring the progressive severity of diabetes-related co-morbidities. This scenario has required the use of new strategies for taking care of the patient by the health professionals responsible for the diabetes care: dietary or pharmacological interventions for weight control, telematic platforms of psychological supports, optimization of glycemic control through hypoglycemic therapies. If access to non-urgent care is more facilitated during phase 2, the limitations, especially for fragile patients with diabetes, persist and therefore it may be essential to maintain alternate telematic consultancy strategies establishing priority criteria for access lists. The metabolic surgery, also, was stopped worldwide limiting the access to an effective treatment and limiting the armamentarium against diabetes [23, 25–27].

About that the DSS (Diabetes Surgery Summit) suggests criteria to help prioritize bariatric and metabolic surgery for when elective surgery is resumed, defining categories of access to surgery based on duration of diabetes, glycemic control, history of cardiovascular disease, presence of chronic kidney disease, non-alcoholic steatohepatitis and obesity-associated symptoms [28].

In our University Diabetes Unit, procedures for remote outpatient check-ups scheduled for over 12,000 patients with diabetes in charge were implemented, in accordance with the organizational proposals of the Italian Diabetes Society [29]. We have adopted strategies ranging from telephone contact to the consultation of the reports recorded and saved in clouds by patients using the CGM (continuous glucose monitoring) up to the use of an App(MySugr) that transmits blood sugar levels directly to our computerized medical record (Smart Digital Clinic) and which is able to automatically make a triage of the urgency of the doctor's intervention in the list of patients requesting an online visit. Over 500 virtual consultations have been performed: patients with a previously scheduled visit have been invited to send blood tests via email to our center and have been contacted by phone to confirm or modify the therapy. The medical staff consulted about a hundred digital glycemic records, communicating extemporaneously with the patient to provide indications for improving glycemic control. Our center was open for over 8 h a day for women with gestational diabetes and for all patients with "urgent" reservations to ensure access to the most complicated cases, assisting more than 100 patients with high priority. The nurses of our Unit carried out bureaucratic tasks such as renewing treatment plans for patients with diabetes.

The fight against diabetes is not only fundamental in preventing the risks to which subjects with diabetes are normally exposed, but in this particular historical moment it is vital for better management of patients infected by SARS-CoV-2, and for limiting the risk of mortality of the patients themselves, both to help reduce the rate of hospitalizations and lighten the burden on the health system caused by this vulnerable population subgroup.

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### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflicts of interest.

**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

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