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## Editorial

# Hyperglycemia and COVID-19: What was known and what is really new?



Diabetes is one of the most relevant co-morbidity in worsening the prognosis of COVID-19 [1]. Data is also showing that hyperglycemia, in both people with or without diabetes, is an important risk factor for death in COVID-19 [2–5]. A. Sing is reporting some important aspects of this finding [2]. In summary, evidence shows:

1. That hyperglycemia in people with diabetes at the time of hospital admission is more relevant as risk factor than the previous glycaemic control evaluated by HbA1c [2]. This evidence emerges particularly from the CORONADO Study (Coronavirus SARS-CoV-2 and Diabetes Outcomes), a French nationwide multicentre observational study, aiming to identify the clinical and biological features associated with disease severity and mortality risk in people with diabetes, hospitalised for COVID-19 [3].
2. That hyperglycemia at the admission in hospital seems worsening the prognosis of COVID-19 more in people without diabetes than in people with diabetes [2].

However, it is worth to mention that glucose variability during the hospitalization, in both diabetes and non-diabetes, also emerged as independent risk factor for a worse prognosis in COVID-19 [4,5].

According to this evidence, it is clear that acute hyperglycemia has a key role as independent risk factor in COVID-19. This evidence has raised a great interest, being considered somehow a new finding. However, how much new is it?

Already, during the previous SARS epidemic, diabetes and hyperglycemia emerged as risk factors for a worse prognosis of the disease [6].

The specific and more relevant role of acute hyperglycemia in diabetes, more than the previous HbA1c, is well known in the Intensive Care Units (ICU), where an increased gap between admission glucose and HbA1 has been found as predictor of mortality in critically ill patients with diabetes [7,8]. The impact of acute (stress) hyperglycemia and glucose variability in critically ill patients is very well known [9]. Moreover, it is also well known that acute hyperglycemia in the ICU is more dangerous for people without diabetes than for people with diabetes [10].

Acute hyperglycemia induces inflammation, endothelial dysfunction and thrombosis, through the generation of oxidative stress [11]. In diabetes chronic hyperglycemia, through

oxidative stress, is inducing an increase of antioxidant defences in the cells therefore, during an acute spike of hyperglycemia the tissues are somehow protected [12]. This is not the case in absence of diabetes, exposing the tissues to more damage. In vitro experiments were able to demonstrate the key role of some miRNAs in this phenomenon [13].

According to what described above, the question is not why hyperglycemia worsens the prognosis of COVID-19, but why it is so frequent. For example, it has been reported that acute hyperglycemia occurs in about 50% of patients hospitalised for COVID-19, while the prevalence of diabetes in the same population was about 7% [14]. A possible hypothesis is that the “Severe acute respiratory syndrome coronavirus 2” (SARS-CoV-2) may affect the pancreatic  $\beta$ -cells producing a reduction of insulin secretion [15]. At the same time, the infection is also accompanied by a huge production of cytokines, which may induce insulin resistance [15]. Both, reduced insulin secretion and insulin resistance, may hesitate in hyperglycemia [15].

In conclusion, the effect of acute hyperglycemia during COVID-19 is not so much surprising and it should be treated according to the already existing guidelines [16–18].

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