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The risk factors potentially influencing risk of serious illness/death in people with diabetes, following SARS-CoV-2 infection: What needs to be done from here

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Since early 2020 the whole world has been challenged by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus coronavirus disease 2019 (COVID-19) and the associated global pandemic [1]. People with diabetes are particularly at high risk of becoming seriously unwell after contracting this virus [2,3]. As yet we do not fully understand the underlying factors which contribute to such risk and their respective contributions to outcomes.

In this regard, Barron *et al.* [4] reported an odds ratio (OR) for in-hospital COVID-19-related death of 2.03 (1.97–2.09) in people with type 2 diabetes mellitus (T2DM). A body of work is emerging in relation to the reasons why people with diabetes are more likely to become seriously unwell and in some cases die following a COVID-19 infection.

Two recent landmark articles [5,6] have brought into sharp focus the factors that mediate increased risk of serious consequences of a COVID-19 infection in relation to hospital admission and mortality for vaccinated individuals and for nonvaccinated individuals in England. For the postvaccination study [6] the risk algorithm explained 74.1% of the variation in time to COVID-19 related death.

An early COVID-19 pandemic study from Mexico [7] concluded that early-onset T2DM conferred an increased risk of hospitalization and obesity conferred an increased

risk for ICU admission and intubation. The predictive score for COVID-19 lethality included age ≥65 years, diabetes, early-onset diabetes, obesity, age <40 years, chronic kidney disease, hypertension, immunosuppression and significantly discriminated lethal from nonlethal COVID-19 cases.

We previously showed that in one area of the UK, the month-by-month mortality rate for people with T2DM was up to 2.2 times higher than that in the same month averaged over the previous 5 years in the early stages of the COVID-19 pandemic, with age the strongest independent predictor of death [8]. Work is continuing to understand how much a previous diagnosis of diabetes type 1 diabetes mellitus (T1DM) or T2DM increases the risk of becoming seriously unwell following a COVID-19 infection vs. absence of diabetes as a diagnosis.

Since these early studies, the advent of treatment of hospitalized patients with Dexamethasone has significantly reduced mortality rates across the world. In patients hospitalized with COVID-19, the use of dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone at randomization [9].

Potential pathogenetic links between the SARS-CoV-2 virus and diabetes include the influence of glucose homeostasis and potentially altered immune status on the progression of the viral infection once established [10]. COVID-19 infection aggravates inflammation and alters immune system responses, leading to difficulties in blood glucose control. COVID-19 infection also increases the risk of thromboembolism and is more likely to induce cardiopulmonary failure in patients with diabetes than in patients without diabetes [11]. All of these mechanisms are now believed to contribute to the poor prognosis of some patients with preexisting diabetes and a COVID-19 infection.

In conclusion, as the COVID-19 pandemic moves into a new phase in Europe and some other parts of the world, much remains to be determined about why having diabetes increases the risk of serious consequences of a COVID-19 infection. The COVID-19 global pandemic poses considerable health hazards, for patients with diabetes.

The estimation of risk will require the combination of population based studies using primary and secondary care data and studies that evaluate the immunologic, metabolic and haematologic response following a COVID-19 infection at both a specific tissue and a whole body level, while keeping in mind that basic strategies such

as optimizing pharmacologic management for patients at elevated cardiometabolic risk, with targeted choice of glucose lowering, antihypertensive and lipid lowering medications are as relevant to current and future research as to everyday clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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