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Commentary

Practical scenarios and day-to-day challenges in the management of diabetes in COVID-19 – Dealing with the ‘double trouble’



S. Charles Bronson

The Institute of Diabetology, Stanley Medical College & Hospital, Chennai, Tamil Nadu, India

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1. The novel pandemic and diabetes

The ongoing COVID-19 pandemic caused by the ‘Severe Acute Respiratory Syndrome Coronavirus-2’ (SARS-CoV-2) has emerged as a major public health crisis throughout the world. Diabetes mellitus ranks high among the co-morbidities that cause an adverse impact on the outcomes of patients with COVID-19. Physicians who are involved in the care of COVID-19 patients with diabetes, are faced with certain practical dilemmas and therapeutic challenges that are discussed below. As diabetes and COVID-19 tend to have a ‘bi-directional adverse impact’ on each other, it would be beneficial for physicians to pay attention to these finer nuances in order to make their approach towards diabetes management in COVID-19 more precise and effective.

1.1. Diabetes in the setting of COVID-19 is a co-morbidity well recognised to adversely affect the prognosis

In the midst of evolving concepts about the pathophysiology of COVID-19, a consistent observation has been that most of the severe cases occur in the elderly sub-group of patients and in those with co-morbidities like cardiovascular diseases (CVD), diabetes, hypertension, lung diseases and immunosuppression [1]. A study on the association of diabetes with COVID-19 related in-hospital mortality

in the UK has shown that about one-third of all deaths occurred in people with diabetes [31.4% in those with type-2 diabetes; 1.5% in those with type-1 diabetes and 0.3% in those with other types] [2]. An epidemiological analysis done in China revealed that the case-fatality rate (CFR) was highest in the >80 years age-group. Those ‘without co-morbidities’ had a CFR of 0.9% whereas those ‘with co-morbidities’ had CFRs as follows – CVD-10.5%, Diabetes-7.3%, chronic respiratory disease-6.3%, hypertension-6.0% and cancer-5.6% [3]. Here, it is noteworthy that diabetes is next only to CVD with respect to the CFR. That diabetes is an established risk factor for CVD is well known.

1.2. Newly diagnosed diabetes in COVID-19

Hyperglycaemia can be detected for the very first time in the setting of COVID-19 (Table 1). Like any other stressful event, COVID-19 can unmask a pre-existing diabetes which would remain even after the disease subsides. Sometimes, a stress hyperglycaemia may evolve during the course of COVID-19 disease and it may revert to normal after the infection has subsided. Iatrogenically, steroids used to treat COVID-19 may induce hyperglycaemia [4] in an individual already prone to develop diabetes due to genetic and environmental risk factors. This hyperglycaemia may either persist to variable degrees after the steroid course is over or revert to normal for the time being. Furthermore, a distinct entity of ‘new-onset diabetes in COVID-19’, that is, diabetes that has arisen ‘de novo’ due to the hypothesized diabetogenic effect of SARS-CoV-2,

E-mail address: dr.s.charlesb@gmail.com

Table 1
The clinical forms of newly detected diabetes in the setting of COVID-19.

S. No.	Clinical type	Probable course after COVID-19 disease subsides
1.	Unmasked pre-existing diabetes.	Continues as overt diabetes.
2.	Stress hyperglycaemia.	Reverts to normoglycaemia.
3.	Steroid-induced hyperglycaemia in an individual prone to develop diabetes.	Either persists after completion of the steroid course or reverts back to normal.
4.	'New-onset diabetes in COVID-19' due to diabetogenicity of SARS-CoV-2 virus.	The course of diabetes in this case is not yet fully understood and is widely investigated.

has been proposed. This potential triggering of diabetes is likely due to the binding of SARS-CoV-2 to the angiotensin-converting-enzyme-2 (ACE2) expressed on the pancreatic beta-cells leading to beta-cell dysfunction and impaired insulin secretion [5].

The physician should note that since this diabetes is first recognised in the setting of an acute infection and especially during a pandemic, careful monitoring, reassessment and characterisation of the type of diabetes is essential after the patient is cured of COVID-19. The patient with newly detected diabetes needs to be educated regarding the necessity of proper follow-up and adherence to anti-diabetic treatment.

1.3. 'Steroid therapy' for COVID-19 amplifies hyperglycaemia to a significant extent

The fact that diabetes complicates an infection is well recognised. Optimal glycaemic control is desirable and essential in the management of any infection in a diabetes patient. This holds true for COVID-19 also.

Based on the severity of disease, COVID-19 patients are likely to receive steroids to improve clinical outcomes. This is especially true for those in the critical care units. A recent trial from Oxford University has shown beneficial effects of dexamethasone in COVID-19 patients, especially in those who were receiving respiratory support [6,7]. Patients with COVID-19 and diabetes who receive steroids like dexamethasone and methylprednisolone are prone to develop extreme rises in blood glucose [4,8], often requiring high doses of insulin. Furthermore, caution should be exercised to avoid hypoglycaemia when the steroid dose is reduced, as this would cause reduction in blood glucose levels correspondingly.

1.4. Precipitation of acute metabolic complications like diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS)

Acute hyperglycaemic complications like DKA and HHS have been observed to occur in enhanced proportions in COVID-19 patients with diabetes- both type 1 and type 2 [9,10]. This trend is also seen in those with newly detected diabetes in COVID-19, sometimes even as the first presentation of hyperglycaemia [10]. These acute glycaemic decompensations add on to the burden of morbidity and mortality due to COVID-19. Prompt recognition and management of DKA and HHS in COVID-19 patients as well as the prevention of these complications whenever possible are critically important to improve outcomes [9].

A plausible hypothesis is that the potential tropism of SARS-CoV-2 to the beta cells results in an acute and rapid impairment of beta-cell function and even destruction of beta-cells, thus precipitating acute hyperglycaemic complications in COVID-19 [11].

1.5. Acute kidney injury (AKI) and the modification of anti-diabetic therapy

In a study conducted in Wuhan, China, evidence of kidney disease was present in nearly 40% of patients admitted with COVID-19. Kidney disease on admission and AKI during hospitalisation were associated with increased mortality [12].

Patients with diabetes who have pre-existing diabetic nephropathy and chronic kidney disease (CKD) may develop an acute exacerbation of CKD during admission for COVID-19. Even those diabetes patients who do not have CKD may develop AKI during hospitalisation. Certain COVID-19 patients who already have 'post-transplant diabetes' after a renal transplant, are likely to be on immunosuppression and might have elevated renal parameters. Furthermore, drugs like remdesivir used in the management of COVID-19 frequently cause AKI and elevated transaminase levels [13].

All such situations call for a careful decision on the choice and dose of the anti-diabetic drugs that could be employed in treatment. The need for insulin arises more often than not.

2. Conclusion

Thus, while COVID-19 is a rampant 'infectious-disease pandemic' that has hit the world hard, diabetes is a relatively silent, yet equally devastating 'non-communicable-disease pandemic' of the modern times. Where both occur together, they present a 'double trouble' as discussed above, to the patient as well as the physician, demanding diligent efforts to be overcome.

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Conflicts of interest

The author declares that he has no conflict of interest.

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