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Editorial

Diabetes Mellitus in Ongoing Covid-19 Pandemic

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Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an ongoing pandemic. As of now, more than 25 million confirmed cases including over 8 lakh death have been reported around the world.

Recent data suggest that most people with COVID-19 have comorbidities, among these the most prevalent of which are diabetes, cardiovascular disease, and hypertension [1]. Researchers have revealed that the endocrine and metabolic conditions are risk factors for acquiring the new coronavirus and care of these patients pose unique challenges in clinical management [2].

With about half a billion people affected, diabetes mellitus (DM) is the leading non-communicable and chronic pandemic disease worldwide. Diabetic individuals have a greater risk of respiratory infections due to compromised immune system, especially the innate immunity [3]. Even transient hyperglycemia may temporarily affect innate immune responses to infection. DM patients are vulnerable to viral infections including novel coronavirus. Depending on the global region, 20 - 50% of patients in the COVID-19 pandemic had diabetes. Patients with diabetes have an increased risk of severe complications including Adult Respiratory Distress Syndrome and multi-organ failure [4]. COVID-19 appears to precipitate severe manifestations of diabetes, including diabetic ketoacidosis (DKA), hyperosmolar hyperglycemic state (HHS), and severe insulin resistance [5-7].

Epidemiological observations showed that the risk of a fatal outcome from COVID-19 is up to 50% higher in patients with diabetes than in those who do not have diabetes [8]. The risk of severe COVID-19 infection is higher if there are other comorbidities like heart and lung diseases.

Diabetic patients have been shown to have an elevated pro-inflammatory cytokine level, in particular IL-1, IL-6 and tumor necrosis factor (TNF)-a [9]. Dysfunctional pro-inflammatory cytokine responses in diabetic patients exaggerate the cytokine storms in COVID-19 leading to a more severe COVID-19 [9-12].

The interaction between Covid-19 and diabetes could be bi-directional, with Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) potentially worsening pre-existing diabetes or even predisposing to diabetes in non-diabetic subjects [13-15]. Fasting glycemia and acute-onset diabetes has been reported among patients with SARS coronavirus (SARS-CoV or SARS-CoV-1) pneumonia [15]. SARS coronavirus receptor, angiotensin-converting enzyme 2 (ACE2) are present in different human tissues like bronchus, lung parenchyma, ileum, testis, and cardiovascular, renal and gastrointestinal tissues, and pancreas [16]. The organ involvements of SARS correlated with organ expression of ACE2. The localization of ACE2 expression in the endocrine part of the pancreas suggests that SARS coronavirus enters islets using ACE2 as its receptor and damages islets causing acute diabetes [17].

Diabetic patients with better-controlled blood glucose had a lower mortality rate than those with poorly controlled blood glucose during hospitalisation [18]. Analysis of national diabetes and mortality data from the United Kingdom before and during the pandemic also

suggests that there is an increase in mortality risk with high glycated hemoglobin (A1C) and the risk increased as A1C levels rose [19]. As primary prevention, patients with diabetes should intensify their metabolic control. This includes continuation and strict abidance with adequate control of blood pressure and lipids.

Patients with diabetes and hypertension treated with ACE inhibitors and angiotensin receptor blockers (ARBs) can have increased expression of ACE2, thereby facilitating viral uptake and increasing the risk of severe infection for people with diabetes [20]. There is, however, no clinical or scientific evidence to suggest that treatment with ACE inhibitors or ARBs should be discontinued because of the COVID-19 infection. It is strongly recommended that physicians and patients should continue treatment with their usual anti-hypertensive treatment [21].

In view of close links between diabetes and cardiovascular disease, statins should not be discontinued because of the long-term benefits and the potential for tipping the balance towards a cytokine storm by rebound rises in interleukin (IL)-6 and IL-1β if they were to be discontinued. Screening for hyper inflammation using laboratory trends (e.g. increasing ferritin, decreasing platelet counts, high-sensitivity C-reactive protein, or erythrocyte sedimentation rate) help to identify subgroups of patients for whom immunosuppression (steroids, immunoglobulins, selective cytokine blockade) could improve the outcome [4].

Although Lactic acidosis associated with metformin, or euglycemic or moderate hyperglycemic diabetic ketoacidosis associated with sodium-glucose linked transporter-2 (SGLT-2) inhibitors are rare events; it is recommended to discontinue for patients with severe symptoms of COVID-19 to reduce the risk of acute metabolic decompensation [22].

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