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Editorial

Resurgence of COVID-19 and diabetes in India



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The second wave of the COVID-19 pandemic has hit India hard. The number of new cases per day has gone up from 11,794 in the first week of February 2021 to over 315,000 as of April 22, 2021. The marked complacency of the population with regard to COVID-19 appropriate behaviors and delayed official responses has primarily been responsible for the resurgence in the cases.

The second wave is different from the first wave in September 2020 in a few ways: first, the rate of increase in new cases is significantly higher. The increase from 10,000 to 80,000 new cases per day from February to April has taken less than 40 days. In September, this journey took 83 days. Second, while the elderly continue to be more vulnerable to COVID-19 in the second wave, a marginal rise has been recorded in the number of young people testing positive for the virus. Third, compared to the first wave, there has been a substantial increase in the proportion of patients presenting with shortness of breath and those requiring oxygen supplementation and mechanical ventilation during the ongoing second wave. Lastly, unlike the first wave, a significant proportion of the cases in the second wave are being caused by SARS-CoV-2 variants, which are believed to be more contagious than the wild-type virus.

As during the first wave of the pandemic, nearly 50% of the patients affected during the second wave harbor at least one comorbidity. Even since the inception of the pandemic, diabetes mellitus has emerged as one of the distinctive comorbidities that has consistently been associated with severe disease, acute respiratory distress syndrome and mortality in COVID-19 [1–3]. In fact, diabetes has been implicated as the most important cause for mortality in COVID-19 hospitalized patients [4].

Furthermore, COVID-19 has been implicated in the development of new-onset diabetes mellitus (NOD) [5]. New-onset diabetes may develop during the acute phase of infection with SARS-CoV-2 or during the post-acute COVID-19 phase, the so-called 'Long COVID'. In a retrospective cohort study of 47,780 discharged COVID-19 patients (mean age 65 years) in England, the rate of NOD was 29 per 1000 person-years over a mean follow-up of 4.6 months [6]. It has been reported from New Delhi, north India, that individuals who were diagnosed with new-onset diabetes during the COVID-

19 pandemic resembles those diagnosed before COVID-19 in symptomatology, phenotype, and C-peptide, although the former subgroup of patients tend to have more severe glycemia than the latter [7].

The second wave of the COVID-19 pandemic is expected to be more unpropitious for patients with diabetes in many ways. First, as the second wave is more severe than the first wave, the disease is also expected to be all the more severe in patients with diabetes. Second, with the resurgence of COVID-19 and cessation of outpatient department services in many healthcare facilities, routine diabetes care is expected to be compromised, leading to suboptimal glycemic control as had been seen at the time of lockdown during the first wave of the pandemic [8,9]. As reflected in an increase in glycated hemoglobin (HbA1c), inappropriate glycemic control would be associated with severe disease and poor outcomes in COVID-19 [10]. Third, as COVID-19 vaccination had hitherto been made accessible only for individuals aged 45 years and above, patients with type 1 diabetes (T1D) and young-onset T2D are more likely to be affected during the second wave.

Fourth, as the second wave is more severe than the first wave, inflammation and cytokine-mediated hyperglycemia are likely to be more marked in COVID-19 patients with diabetes. Hyperglycemia at admission and during hospitalization is consistently associated with poor outcomes in COVID-19 patients [11]. Fifth, with moderate-to-severe disease being more predominant during the ongoing second wave, more patients are likely to be administered corticosteroids. However, it is unclear whether corticosteroid-related worsening of in-hospital dysglycemia would negate the mortality benefits in COVID-19 patients with diabetes mellitus.

Sixth, there are theoretical concerns of COVID-19 reinfections in patients with diabetes mellitus [9,12]. With the emergence of new SARS-CoV-2 variants, reinfections are more likely, especially with the immune-escape "double" and "triple" variants. Because pulmonary diffusion capacity is impaired even after 6 months of the onset of illness in more than 50% of COVID-19 survivors with severe disease [13], reinfection in a diabetic patient recuperating from a prior COVID-19 infection can be no less than a disaster. Lastly, it is unknown whether the new variants could have any additional direct detrimental effect on the pancreatic β -cells, thereby predisposing COVID-19 patients to an increased risk of NOD.

Considering the fact that all the odds are stacked against the diabetic subpopulation, it is imperative that they take extra precautions and stringently adopt COVID-19 appropriate behavior. Staying indoors, appropriate hand hygiene, use of facemasks, and maintaining appropriate physical distance from others while venturing outdoors should be the norm [14]. Mask fit and filtration can be improved by using two facemasks, such as a cloth mask over a medical procedure mask. Good glucose control should be strived

for, and whenever possible, virtual consultation with physicians would help fine-tune the glycemic profile [15,16].

There exists no robust evidence to support the use of one anti-diabetic drug over the other. A large nationwide observational study conducted in England had concluded that there was no clear indication to change prescribing of glucose-lowering drugs in patients with type 2 diabetes (T2D) amid the ongoing pandemic [17]; however, preliminary data suggest that dipeptidyl peptidase-4 inhibitors (DPP4i) might improve clinical outcomes in COVID-19 patients with T2D [18]. Notably, however, the DARE-19 randomized controlled trial found that dapagliflozin was not beneficial in adult patients hospitalized with COVID-19. Besides, most patients with T2D are expected to be on statins, and continuation of statin therapy has been shown to benefit patients with COVID-19 [19]. Lastly, and perhaps of utmost importance, in the absence of any absolute contraindication, all patients with diabetes mellitus (aged 18 years and above) should get vaccinated against COVID-19 sooner rather than later [20].

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Conflicts of interest

None to declare.

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