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Editorial Commentary

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# COVID-19 and the surge in youth diabetes: Fleeting effect or lasting consequence?

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The COVID-19 pandemic, caused by the novel coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), emerged in late 2019. The virus, first identified in Wuhan, China, quickly spread across international borders, leading to widespread outbreaks in nearly every country, leading to widespread illness, significant loss of life, and overwhelming strain on healthcare systems.<sup>[1]</sup> By early 2020, COVID-19 was declared a pandemic by the World Health Organization.<sup>[1]</sup> While the immediate focus was on respiratory complications, evidence soon emerged that COVID-19 could trigger or exacerbate various other health conditions, including metabolic and autoimmune disorders.<sup>[2,3]</sup> One such condition is diabetes mellitus, including both type 2 diabetes (T2D) mellitus, a metabolic disorder, and type 1 diabetes (T1D) mellitus, an autoimmune disorder.

A large number of studies have reported a higher incidence of diabetes mellitus in youth during the COVID-19 pandemic. A similar trend was reported for both T1D and T2D. A meta-analysis revealed, in comparison with the pre-pandemic year, a 14% and 27% increase in the incidence rates of T1D in the pandemic years 1 and 2, respectively.<sup>[4]</sup> These incidence rates were remarkably higher than the usual 2% annual increase in the incidence rate of T1D during the pre-pandemic period. The incidence rates of T2D increased were much greater (62–470%).<sup>[5-10]</sup> However, caution was raised to interpret these trends to avoid overestimation of the incidence during the COVID-19 pandemic, which may result from under-seeking of care during the immediate pre-pandemic or early pandemic period. Nonetheless, the comparison with the trends over a longer duration of pre-pandemic and pandemic periods in some studies strengthens the occurrence of a true increase in the incidence.<sup>[10]</sup>

A study published by Montgomery *et al.* reported increased incidence rates of new-onset T1D (11%) and T2D (238%) in youth from the United States than those in the pre-pandemic period and reiterated the observations from most of the previous studies.<sup>[11]</sup> A striking increase in T2D than that of T1D is mostly attributed to increased body mass index (BMI) due to forced sedentary lifestyle during the pandemic.<sup>[8]</sup> However, the reasons for the increased incidence rates of T1D are intriguing. Although a direct effect of the virus on  $\beta$ -cells of pancreatic islets was initially proposed as a potential cause for the increased incidence of T1D during the pandemic, it remains futile.<sup>[12,13]</sup> Another possible reason could be increased rates of obesity, even in T1D. The accelerator hypothesis, although not widely accepted, proposes earlier manifestation of T1D in obese individuals.<sup>[14,15]</sup> A study from Germany also reported an association between increased time-varying BMI and overweight risk at 9 months of age during the COVID-19 pandemic and their association with increased risk for developing islet autoimmunity in children at increased risk for T1D.<sup>[16]</sup> Another

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plausible mechanism is the triggering of autoimmunity by SARS-CoV-2. Studies have reported an increased frequency of islet-related antibodies as well as other-organ related antibodies in newly diagnosed T1D children during the COVID-19 pandemic than those in the pre-pandemic period.<sup>[6,17-20]</sup> However, this observation is inconsistent;<sup>[21,22]</sup> Hence, the reasons for higher incidence rates of T1D during COVID-19 are unclear and likely multifactorial.

Besides increased incidence rates of diabetes mellitus in youth, higher rates of diabetic ketoacidosis (DKA) and presentation with severe DKA are also reported during the pandemic.<sup>[23]</sup> This was observed among youth with both T1D and T2D.<sup>[6]</sup> A higher prevalence of hyperosmolar coma was also noted among youth with T2D. More frequent presentations with severe disease were attributed to delay in seeking health care. Unlike the majority of the studies, there was no increased frequency of DKA among youth with T1D and T2D; however, the frequency of severe DKA among youth with T1D was greater than the pre-pandemic period but not in those with T2D. Interestingly, youth with T2D were younger during the pandemic than in the pre-pandemic period, which suggests an earlier onset of T2D in youth. However, this observation was not found in the majority of the studies.<sup>[5,6,9,10]</sup> Mefford et al. indeed reported a 28% decrease in the incidence rate of T2D during the pandemic in children younger than 9 years.<sup>[10]</sup> However, in the study by Sasidharan Pillai et al., the age at onset of T2D was significantly lower during the pandemic year 1 but not during the pandemic year 2 than the pre-pandemic period.<sup>[5]</sup> A study by Magge et al. reported significantly higher BMI of youth diagnosed with T2D during the pandemic (34.3 vs. 35.1 kg/m<sup>2</sup>).<sup>[23]</sup> Surprisingly, most of the studies, including Montgomery et al., have not reported a greater BMI of youth with T2DM during the pandemic period despite the increased incidence rate.<sup>[5,10,11]</sup> This may be due to a specific threshold of BMI for the development of T2D in youth. Indeed, an increase in the BMI z-score of these individuals from the pre-pandemic to the pandemic period might have occurred but is not well studied.

Typically, a higher incidence of T1D was noted during the winter seasons in the pre-pandemic years.<sup>[24]</sup> In contrast, Montgomery *et al.* reported the peak incidence rates of T1D in the summer seasons of both the pandemic years (2020 and 2021).<sup>[11]</sup> A similar trend has also been reported in other studies from Europe and North America, with a peak incidence rate during the summer season in the pandemic year 1.<sup>[20,25-28]</sup> Notably, the seasonal trend in the incidence rate of pediatric T1D returned to the pre-pandemic pattern in Europe during pandemic year 2 but not in North America, where the incidence rate peaked during the last months of 2021.<sup>[25]</sup> In contrast to the latter observation, the study by Montgomery *et al.* from the United States reports a peak incidence rate of T1D during the spring-summer of pandemic year 2, with a gradual

decline subsequently.<sup>[11]</sup> Interestingly, the seasonal variations were less pronounced for pediatric T2D. A large study from the United States demonstrated a gradual increase in the incidence rates of T2D beginning in the third quarter of 2020, with peak incidence rates during the last quarter of 2020 and the first two quarters of 2021, with a gradual decline thereafter.<sup>[10]</sup>

As a novel observation, Montgomery et al. also reported a decline and stabilization of the incidence of T1D and T2D in youth in 2022.<sup>[11]</sup> Several such reports have emerged recently. Grundman et al. also reported higher incidence rates of T2D in youth from the United States (18.7 cases/month) during the pandemic year 1 that declined during the pandemic year 2 (4.3 cases/month) to pre-pandemic incidence rates (3.9 cases/month).<sup>[8]</sup> The authors attributed to the increased incidence rate during the pandemic year 1 to virtual learning. In another recent study from the USA, Kim et al. reported higher incidence rates (cases/month) of T2D in youth in the pandemic years 1 (20.1  $\pm$  6.0) and 2 (25.9  $\pm$  8.9), which declined in the subsequent year  $(14.5 \pm 4.1)$  near to that in the pre-pandemic year  $(11.8 \pm 3.7)$ .<sup>[7]</sup> Such trends have also been reported for T1D. In a study from Scotland, the incidence rate of T1D in 6-14-year-old children peaked around early 2021, followed by a gradual decline to pre-pandemic incidence rates by mid-2022 with stabilization thereafter.<sup>[29]</sup> Hence, the effect of the COVID-19 pandemic on the incidence rates of T1D and T2D in youth is transient. However, more long-term data are required to understand the long-term impact of the pandemic on the incidence rate of diabetes in youth.

# **Ethical approval**

Institutional Review Board approval is not required.

#### Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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## **Conflict of interest**

There are no Conflict of Interest.

# Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of Artificial Intelligence (AI)-Assisted Technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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