

Is type 1 diabetes related to coronavirus disease 2019 in children?

Minsun Kim, MD, PhD^{1,2}

¹Department of Pediatrics, Jeonbuk National University Medical School, Jeonju, Korea; ²Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, Jeonju, Korea

Key message

- Evidence shows that patients with type 1 diabetes have been severely affected by coronavirus disease 2019 (COVID-19) in various ways.
- Although there is no reliable evidence that COVID-19 worsens or induces diabetes, it can impair β -cell insulin secretion and glucose control by inducing inflammation and cytokine production.
- A study is needed of the short- and long-term relationship between diabetes and COVID-19 in the Korean pediatric population.

Since the onset of the coronavirus disease 2019 (COVID-19) pandemic, many diabetes researchers have reported a relationship between COVID-19 and type 2 diabetes.¹⁾ However, recent reports on COVID-19 in children and adolescents with type 1 diabetes mellitus (T1DM) have provided insufficient evidence. Most studies have focused on mortality, morbidity, and management after COVID-19 in patients with diabetes.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) acutely or chronically confuses the epidemiology of T1DM. This is because some viral illnesses cause or augment T1DM. To date, many studies have suggested that SARS-CoV-2 infection is unlikely to induce autoimmunity or cause permanent β -cell damage.²⁾

Early studies reported that the incidence of T1DM increased simultaneously with the COVID-19 pandemic.²⁾ However, this was not the case in late population-based data reports.^{2,3)} In other reports, shutdown in primary care institutions and the main opening of acute care centers delayed the diagnosis and treatment of patients and caregivers, and many patients already had acute disease upon arriving at the hospital.^{2,3)}

Cytokine storm, commonly found in COVID-19, can damage or knock out limited β -cell storage in individuals close to stage 3 T1DM, accelerating the last week of acute disease onset, but this has not been confirmed.²⁾ Although there is no reasonable proof that SARS-CoV-2 aggravates or causes persistent diabetes, COVID-19 may trigger inflammation and cytokine production,

leading to impaired β -cell insulin secretion and glucose control.²⁾

The damage to β cells caused by the virus is due to (1) the direct dissolution effect of viral replication; and/or (2) damage through the inflammatory reaction of the host by auto-reactive CD+ T cells leading to autoimmune diseases.¹⁾

Several viral infections have been suspected to cause clinically obvious T1DM as a possible trigger for the autoimmune process and may accelerate the clinical incidence of the at-risk subject.^{4,6)}

COVID-19 reportedly causes serious metabolic disorders, such as diabetic ketoacidosis and hyperglycemic hyperosmolar state in patients with existing or new-onset diabetes.¹⁾ Moreover, some researchers have suggested that SARS-CoV-2 causes T1DM onset.⁶⁾ Damage to pancreatic islet cells by the coronavirus is highly probable and does not appear to be a new phenomenon in existing virus-related studies.⁷⁾ In addition, more than 90% destruction of β cells by direct virus-mediated injury causes nonauto-immune diabetes, but limited lysis releases pancreatic islet cell antigens and enhances the autoimmune response.¹⁾

Recent viral data have demonstrated that the angiotensin-converting enzyme (ACE) 2 receptor is used for host cell entry as an important commonality between SARS-CoV-2 and SARS-CoV-1 infections.^{8,9)} Compared to SARS-CoV-1, SARS-CoV-2 is significantly more contagious, and it is speculated that it can cause stronger infection of ACE2+ cells using adhesion factors with higher efficiency.⁴⁾ ACE2 mRNA expression has been observed in pancreatic and other tissues (nasal epithelium, lung, gastrointestinal system, testis, cardiovascular, renal, etc.).^{1,9)} There may be a bidirectional link between COVID-19 and pancreatitis-induced diabetes.

In recent studies of children and adolescents, evidence was lacking that the presence of diabetes is associated with a higher risk of contracting COVID-19 than the absence of diabetes. In addition, no reports suggest that diabetes is a comorbidity associated with poor outcomes in children and adolescents unlike in adults.⁴⁾

However, given that various subtypes of T1DM have been reported, additional surveillance is needed to determine the status, course, and long-term possibility of developing T1DM in

some children and adolescents after SARS-CoV-2 infection.

COVID-19 is a ruthless disease and catastrophe that mankind has never before experienced. Hyperglycemia appears to increase the COVID-19-associated mortality and morbidity; however, the SARS-CoV-2 virus itself induces or deteriorates hyperglycemia, which can lead to the worst condition.¹⁾ There are challenges to be solved regarding newly developed diabetes related to COVID-19 in children and adolescents. In short, further research is needed to determine whether COVID-19 is related to an increased incidence of diabetes and the involved mechanism in childhood, whether diabetes is a new form of diabetes, β -cell damage is temporary, and it can cause chronic infection in β cells or type 1 diabetes in the long term.¹⁾ How COVID-19 affects the long-term course of preexisting children with diabetes is also an important research topic.

In Korea, the incidence of COVID-19 in children and adolescents is increasing. Short- and long-term data on children and adolescents in Korea should be accumulated and epidemiologically studied in the future.

See the article “Diabetic ketoacidosis in children induced by coronavirus disease (COVID-19) DKA post-COVID-19 in children” via <https://doi.org/10.3345/cep.2021.00941>.

Footnotes

Conflicts of interest : No potential conflict of interest relevant to this article was reported.

ORCID:

Minsun Kim  <https://orcid.org/0000-0002-3617-7823>

References

1. Boddu SK, Aurangabdkar G, Kuchay MS. New onset diabetes, type 1 diabetes and COVID-19. *Diab Metab Syndr* 2020;14:2211-7.
2. DiMeglio LA. COVID-19 and type 1 diabetes: addressing concerns and maintaining control. *Diabetes Care* 2021;44:1924-8.
3. Dayal D, Gupta S, Raithatha D, Jayashree M. Missing during COVID-19 lockdown: children with onset of type 1 diabetes. *Acta Paediatr* 2020;109:2144-6.
4. d'Annunzio G, Maffei C, Cherubini V, Rabbone I, Scaramuzza A, Schiaffini R, et al. Caring for children and adolescents with type 1 diabetes mellitus: Italian Society for Pediatric Endocrinology and Diabetology (ISPED) statements during COVID-19 pandemic. *Diabetes Res Clin Pract* 2020;168:108372.
5. Thakur N, Rai N. Diabetic ketoacidosis in children induced by coronavirus disease 2019 (COVID-19) diabetic ketoacidosis post-COVID-19 in children. *Clin Exp Pediatr* 2021 Nov 30. <https://doi.org/10.3345/cep.2021.00941>. [Epub].
6. Unsworth R, Wallace S, Oliver NS, Yeung S, Kshirsagar A, Naidu H, et al. New-onset type 1 diabetes in children during COVID-19: multicenter regional findings in the U.K. *Diabetes Care* 2020;43:e170-1.
7. Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. *Acta Diabetol* 2010;47:193-9.
8. Hoffmann M, Kleine-Weber H, Schroeder S. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell* 2020;181:271-80.
9. Egloff C, Vauloup-Fellous C, Picone O, Mandelbrot L, Roques P. Evidence and possible mechanisms of rare maternal-fetal transmission of SARS-CoV-2. *J Clin Virol* 2020;128:104447.

How to cite this article: Kim MS. Is type 1 diabetes related to coronavirus disease 2019 in children? *Clin Exp Pediatr* 2022;65:252-3. <https://doi.org/10.3345/cep.2021.01760>