

CORRESPONDENCE



SARS-CoV-2 — No Increased Islet Autoimmunity or Type 1 Diabetes in Teens

TO THE EDITOR: An increased incidence of pediatric type 1 diabetes during the coronavirus disease 2019 (Covid-19) pandemic has been widely reported.¹⁻⁴ We conducted a study involving 4586 children 9 to 15 years of age from the United States, Sweden, Finland, and Germany.⁵ The children were followed from January 2020 (pre-pandemic) through December 2021 (pandemic) and were tested every 3 months for type 1 diabetes if they had islet autoantibodies (440 participants) and every 6 months if they did not (4146 participants) (Table 1). The children were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleocapsid (infection) and spike (vaccination) antibodies at each follow-up visit.

Of the 4586 children, 705 (15.4%) had a positive test for SARS-CoV-2 nucleocapsid antibodies — 623 of the 4146 children without islet autoantibodies (15.0%; 95% confidence interval [CI], 13.9 to 16.1) and 82 of the 440 children with islet autoantibodies (18.6%; 95% CI, 15.0 to 22.3). Among the 4146 children without islet autoantibodies, seroconversion to persistent, confirmed positivity for islet autoantibodies occurred in 40 (1.0%; 95% CI, 0.7 to 1.3). Only 5 of these 40 children had nucleocapsid antibodies, which appeared after seroconversion. The remaining 35

children never had a positive test for nucleocapsid antibodies. Hence, seroconversion did not occur in any children without islet autoantibodies who had had SARS-CoV-2 infection (0 of 623 children); seroconversion occurred only in children without islet autoantibodies who had not had SARS-CoV-2 infection (40 of 3523 children [1.1%; 95% CI, 0.8 to 1.5]).

A total of 45 children received a diagnosis of type 1 diabetes during the 24-month follow-up. Five children received a diagnosis before they had a positive test for SARS-CoV-2 nucleocapsid antibodies. One child received a diagnosis of type 1 diabetes after the detection of SARS-CoV-2 infection. The remaining 39 children with type 1 diabetes never had a positive test for nucleocapsid antibodies: 30 were never vaccinated, 2 were vaccinated before the diagnosis of type 1 diabetes, and 4 were vaccinated after the diagnosis; 3 were not tested. There was no evidence showing that the number of children in whom seroconversion to persistent islet-autoantibody positivity occurred was greater among those with SARS-CoV-2 infection, even with the inclusion of samples obtained after the study period if the last sample within the study period was positive for Covid-19 or islet autoantibodies. The number of children who received a diagnosis of type 1 diabetes did not differ between those with and those without SARS-CoV-2 infection. All the children were seen either four or eight times over the 2 years, depending on islet-autoantibody status.

Despite the plausibility of a biologic connection, systematic testing for the virus and type 1 diabetes in a prospective, multinational cohort of children before and during the pandemic did not show that Covid-19 precipitated type 1 diabetes, in contrast to studies in which Covid-19 testing was not

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performed. These findings must be tempered somewhat because they reflect a narrow age range among children with an increased genetic risk of type 1 diabetes (representativeness of the study cohort is shown in Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). Longer follow-up may provide additional insights.

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Table 1. Characteristics of Children Tested for Covid-19 and followed from January 1, 2020, to December 31, 2021.

Characteristic	All Children	Children with Covid-19
	no.	no. (%)
Sex		
Female	2264	340 (15.0)
Male	2322	365 (15.7)
Age — yr		
9	161	29 (18.0)
10	1059	190 (17.9)
11	934	153 (16.4)
12	974	177 (18.2)
13	840	129 (15.4)
14	590	27 (4.6)
15	28	0
Country		
United States	1829	351 (19.2)
Finland	1053	27 (2.6)
Germany	233	10 (4.3)
Sweden	1471	317 (21.5)
First-degree relative with type 1 diabetes		
No	4066	632 (15.5)
Yes	520	73 (14.0)
Body-mass index*		
≤15	416	63 (15.1)
16–20	2549	395 (15.5)
21–25	1058	165 (15.6)
26–30	275	40 (14.5)
31–35	65	11 (16.9)
36–40	20	6 (30.0)
41–45	3	0
Missing data	200	19 (9.5)
Persistent, confirmed positivity for islet autoantibodies at study start		
No	4146	623 (15.0)
Yes	440	82 (18.6)

* The body-mass index is the weight in kilograms divided by the square of the height in meters. Covid-19 denotes coronavirus disease 2019.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

The data sets generated and analyzed during the current study will be made available in the National Institute of Diabetes

and Digestive and Kidney Diseases Central Repository at <https://repository.niddk.nih.gov/studies/teddy>.

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