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

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.

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

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