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A nationwide survey of Italian pediatric diabetologists about COVID-19 vaccination in children and adolescents with type 1 diabetes

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Type 1 and type 2 diabetes are a cumulative risk factor for both morbidity and mortality from COVID-19 [1]. Luckily, most children with type 1 diabetes and COVID-19 have only mild symptoms or no symptoms at all [1], and children with type 1 diabetes infected with SARS-CoV-2 appear to have similar disease outcomes to peers without diabetes. However, children with COVID-19 with or without underlying conditions can develop multisystem inflammatory syndrome in children (MIS-C) a serious and potentially life-threatening sequela that leaves most children developing the condition needing in-hospital care, sometimes in intensive care units (ICUs) [2].

Currently, the US Food and Drug Administration and the European Medicines Agency have approved the Pfizer/BioNTech and Moderna vaccines for children aged 12 years and older. In Italy, the Pfizer/BioNTech vaccine was authorized in this age group at the end of May 2021 and the Moderna vaccine in July 2021.

There are no data available on COVID-19 vaccination in children and adolescents with type 1 diabetes. We therefore conducted a cross-sectional electronic survey of pediatric endocrinologists and diabetologists in Italy to provide insights into the COVID-19 vaccine in pediatric patients with type 1 diabetes. We also investigated the COVID-19 vaccination status of the responders, and the side-effects they experienced. The survey was conducted from September 1 to September 15, 2021, in pediatric endocrinologists belonging to the Diabetes Study Group of the Italian Society for Pediatric Endocrinology and Diabetes (ISPED) pediatric diabetes centers invited through direct message or email. Although the survey may have been susceptible to sampling and response bias due to the online format, ISPED has nationwide coverage and is therefore likely to be highly representative of the Italian type 1 pediatric diabetes population.

Of the 68 centers belonging to ISPED, 57 (85%) completed the web-based survey and returned complete data, while in six centers two physicians completed the survey each (total number of survey answers 63), but data were only counted once. All the ISPED tertiary referral centers ($n = 39$) responded, and there was no difference between centers who completed and those who did not complete the survey, since the latter only care for few patients each (< 20 patients/center).

Among the 63 diabetologists who answered the survey, all had undergone vaccination with the two doses available

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Table 1 Demographics and vaccination status in responders and the children and adolescents with type 1 diabetes and their parents

Variable	Numbers (percentage) or percentage (median – IQR)
Centers ($n=57$)	
Academic	16 (28%)
Public	37 (65%)
Private	4 (7%)
Do you recommend vaccination for your patients?	
Yes, for 12 years old and older	63(100%)
No	0 (0%)
How many of your patients have been vaccinated?	
12–15 years old	75% (50%; 82.5%)
16–18 years old	100% (75%; 100%)
19–25 years old	100% (100%; 100%)
Did your patients have severe adverse side-effects?	
Yes	$n=3$ (1 myocarditis, 1 loss of consciousness needing ICU admission, 1 anaphylactic reaction), an estimated rate of 0.04%
Did your patients have mild/moderate side-effects?	
Yes	40/53 centers (70%)
Injection site pain	55%
Fever	50%
Headache	30%
Weakness/Asthenia/Myalgia	55%
Glycemic imbalance	2.5%
No	13/53 centers (30%)
How many of your patients' parents have been vaccinated?	75% (75%; 100%)
How many of your patients' parents did not want their children vaccinated?	20% (15%; 25%)

at the time of survey. None reported severe side-effects, while 36 reported injection site pain (57%), 27 fever (43%), 22 headache (35%), 6 weakness or asthenia (17%), and 8 myalgia (22%).

Patients undergoing vaccination were older than 12 years of age (at the moment of the survey, COVID-19 vaccination was not yet cleared for patients 5–11-year-old), and only 20% of parents were anti-vaccination, mainly due to being worried about side-effects (especially long-term ones) or because they thought that their children did not need vaccination due to COVID-19 being mild or asymptomatic in children (Table 1). At the time of the survey, no child of the 20% vaccine-skeptic parents had been vaccinated. Only three patients were reported to have severe adverse side-effects (one myocarditis, one loss of consciousness needing ICU admission, and one anaphylactic reaction, all of whom fully recovered in a few days). This corresponded to an estimated prevalence of 0.05% (calculated according to a total number of patients older than 12 years in the responder centers (n = 7,511) and a minimum vaccination rate of 75% of children older than 12), in line with published data [3]. Mild/moderate side-effects were reported by 70% of patients vaccinated (Table 1). The vaccination rate in patients with type 1 diabetes older than 12 years of age was significantly higher than that recorded for health peers during the same time frame (data from Istituto Superiore di Sanità) (79.5% vs. 62.4%, $p<0.01$), probably because patients with diabetes are considered fragile and at higher risk of morbidity and mortality due to the COVID-19, even if this fact has not been confirmed in pediatric patients [1].

We believe that these data, even if survey-based, maybe useful for devising behavior guidelines for the at-risk population of children and adolescents with type 1 diabetes. Moreover, these data question current recommendations in some European countries advising against vaccination for children 12–15 years of age. The vaccination has few severe adverse side-effects and, when they do occur, recovery is fast. Although common, mild to moderate side-effects, usually injection site pain and fever, last only 24–48 h, making the vaccine safe enough for 12–18-year-olds with type 1 diabetes. While data on COVID-19 vaccine efficacy and antibody responses in children will no doubt emerge over the coming months, our data about vaccine safety in children with type 1 diabetes provide optimism. A recent paper about vaccine diffidence [4], which is a known obstacle to COVID-19 vaccination campaigns, found that 92 out of 502 subjects enrolled

(18.3%) were vaccine hesitant. This percentage is consistent with the opinions of our parents, suggesting that vaccination diffidence is not negligible and needs to be addressed with specific information campaigns to sustain vaccination, especially now that the COVID-19 vaccine has also been approved for children between 5 and 11 years of age, albeit at a different dose (0.2 ml containing 10 μg of SARS-CoV-2 spike protein mRNA compared with 0.3 ml containing 30 μg of mRNA in the vaccine for older children). Interim findings indicate that the vaccine's efficacy against symptomatic disease and its immunogenicity are similar in this age group to those reported for adolescents and young adults. Local reactions were very common, mostly mild to moderate in severity, and might be more frequent than in older children. There were no cases of myocarditis or pericarditis or any other serious adverse event. About five million children 5–11 years of age have now been vaccinated in the USA without any severe adverse events reported, suggesting a highly safe and effective vaccine in this age group [5].

With the controversial landscape of child immunization (from both the political and parent perspectives), these data provide support that, even if specific jurisdictions do not approve the vaccine in all children, then the at-risk population can be safely prioritized and immunized.

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Author's Contribution AES conceived the study and drafted the survey. VC, RS and IR supervised the survey. Contributors listed in the Appendix collected data. AES drafted the report. AES managed the data and performed the statistical analysis. IR and AES wrote the final version of the report. VC, RS and contributors collaborated in the interpretation of the results and discussing and revising the report.

Declarations

Conflict of interests VC serves on the advisory board for Insulet and Eli Lilly, and his institution has received research support from AstraZeneca, Eli Lilly, and Dompè. DL has spoken for Abbott and has received support for attending meeting from Eli Lilly. IR serves on the advisory board for Sanofi Aventis and Movi and has spoken for Aboca, Abbott, Sanofi Aventis and Eli Lilly. RS has spoken for Abbott and Lilly, has received support for attending meeting from Medtronic and Movi, and has served on advisory boards for Abbott and Sanofi. AES has spoken for Sanofi and Abbott, has received support for attending meeting from Movi and has served on the advisory board for Medtronic and Movi.

Human and Animal Rights The study was approved by the coordinating center Ethical Committee (ASST Cremona) and conducted according to the Declaration of Helsinki.

Informed consent All participants gave their informed consent to answer the survey.

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