


COVID-19 vaccination in adolescents and young adults with type 1 diabetes: Glycemic control and side effects

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Abstract

Background: Two vaccines against SARS-CoV-2 are approved by the World Health Organization (WHO) for minors aged 12 years and over. Currently, people with both type 1 diabetes (T1D) and type 2 diabetes (T2D) are prioritized for vaccination.

Objective: To evaluate possible glycemic control modification, insulin dose adjustment and adverse effects after COVID-19 vaccination in young T1D individuals, users of different technology levels.

Methods: Thirty-nine T1D individuals, who received a whole vaccination cycle of either Moderna or Pfizer-BioNTech vaccines, were enrolled, 24 of whom using advanced hybrid closed loop systems (AHCLs) and 15 using intermittently scanned continuous glucose monitoring (isCGM). Symptoms after each dose and the following variables were considered: time in range 70–180 mg/dl (TIR), time in different glucose ranges, mean glucose levels, coefficient of variation (CV), total daily dose (TDD) and bolus proportion

Results: No significant differences in TIR, time in different glucose ranges, mean glucose levels, TDD, bolus proportion, were observed before and after any dose nor before and after the whole vaccination cycle. CV was significantly lower after the whole vaccination cycle (CV pre-vaccination $35.1 \pm 6.9\%$ vs. CV post-vaccination $33.5 \pm 6.3\%$; p 0.031) in subjects treated by AHCLs. Side effects after the vaccination were mild and more frequent after the second dose. No severe adverse reactions were reported.

Conclusions: COVID-19 vaccination was safe and not associated with significant perturbation of glycemic control in adolescents and young adults with T1D. This information could be of clinical use when counseling families about SARS-CoV-2 vaccination in young people with T1D.

KEYWORDS

advanced hybrid closed loop, children, COVID 19 vaccination, metabolic control, type 1 diabetes

1 | INTRODUCTION

In December 2019 in Wuhan, China, a new infectious disease began to spread: Coronavirus Disease 2019 (COVID-19). The number of cases of the disease, caused by the Severe Acute Respiratory Syndrome Corona

Virus 2 (SARS-CoV-2), rapidly increased worldwide, so that the World Health Organization declared a pandemic on March 11, 2020.¹

The impact of the disease in the pediatric population has been lower, accounting for 1%–5% of COVID-19 cases, often pauci/asymptomatic and deaths have been extremely rare.²

However, the potential long-term effects in children are still unknown and multisystem inflammatory syndrome in children (MIS-C) can occur even after a mild infection.³ Moreover, children play a major role in disease transmission.⁴

Several reports have described greater morbidity and mortality from COVID-19 in people with diabetes, especially when accompanied by obesity.⁵ Most of this information comes from studies on individuals with type 2 diabetes (T2D), and applying the same concepts to type 1 diabetes (T1D) could be misleading. Furthermore, COVID-19 was recently observed to be more severe in T1D than in healthy people if a poor glycemic control exists. On the other hand, age is still the strongest risk factor for illness severity and communications neglecting the role age plays may inappropriately raise concerns.⁶

These findings emphasize the importance of prioritizing COVID-19 vaccination in people with diabetes.⁷ Since the beginning of the pandemic, only a handful of vaccines have been tested in young people over the age of 12, including mRNA vaccines made by Moderna and Pfizer-BioNTech.

At the time of writing, in Italy, more than 2 million people with an age between 12 and 19 years have been vaccinated with at least one dose⁸ and the safety and impact of the COVID-19 vaccination in youth with T1D is now a matter of great importance.^{9,10}

To our knowledge, there are no published studies about the effect of the whole COVID-19 vaccination cycle on glycemic control in adolescents and young adults with T1D.

In this study, we evaluated adverse effects, possible glycemic control modification and temporary insulin dose adjustment in youth with T1D, users of different levels of technology, who completed a whole COVID-19 vaccination cycle.

2 | METHODS

In this retrospective study, 39 T1D individuals older than 16 years of age who underwent a whole vaccination cycle of either Moderna or Pfizer-BioNTech vaccines between March and June 2021 were considered. Twenty-four were being treated by advanced hybrid closed loop

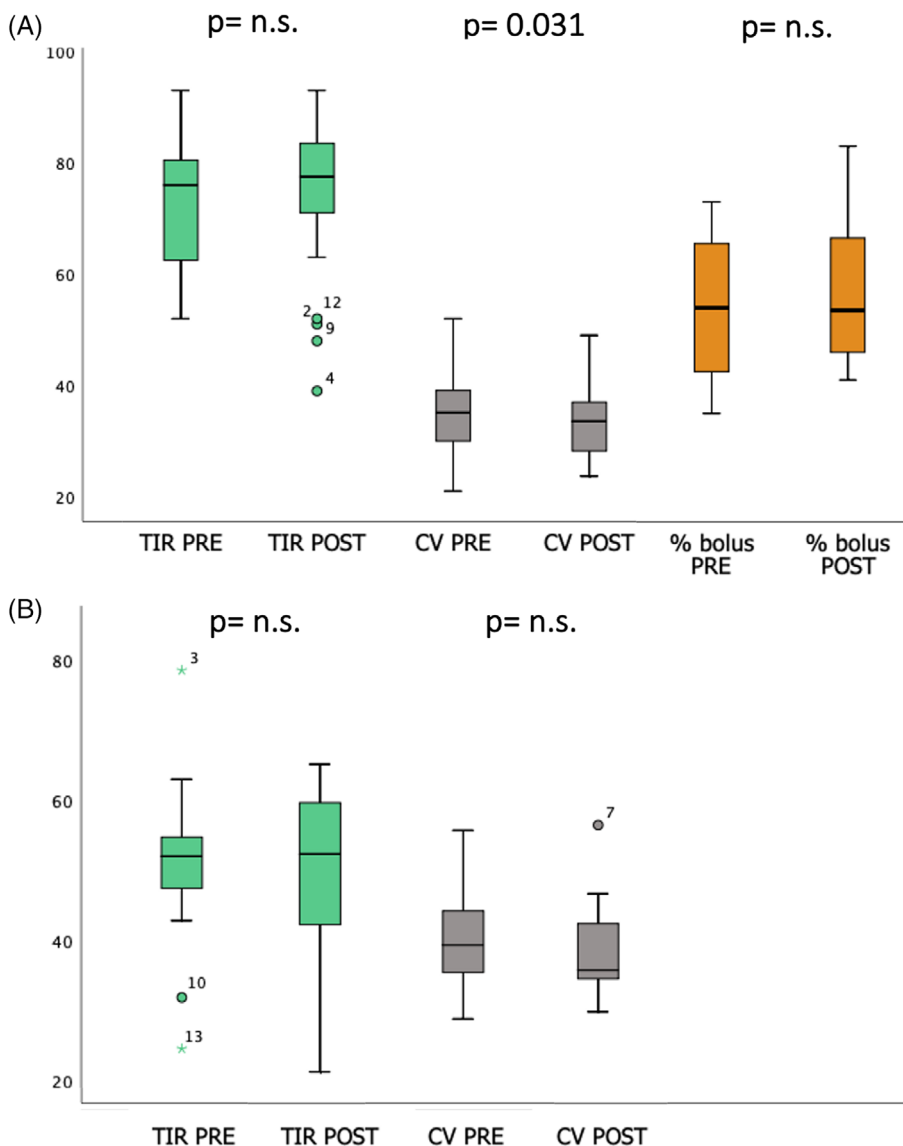


FIGURE 1 Boxplots for TIR (green) and CV (gray) before and after the whole vaccination cycle in (A) patients with AHCL and (B) patients with isCGM. For patients with AHCL, the bolus insulin proportion (orange) before and after vaccination is also depicted. The only significant difference was between pre- and post- vaccination CV in patients with AHCL. AHCL, advanced hybrid closed loop; CV, coefficient of variation; isCGM, intermittently scanned continuous glucose monitoring; TIR, time in range

systems (AHCLs), 12 with Tandem t:slim X2 with Control IQ technology and 12 with Medtronic 780G SmartGuard auto mode. Fifteen were using intermittently scanned continuous glucose monitoring (isCGM) and were being treated either by multiple daily injections (MDI 9) or continuous subcutaneous insulin infusion (CSII). We retrospectively investigated symptoms after first and second dose recorded in medical files during the outpatient visits, either face to face or via telemedicine, and analyzed the following variables based on current recommendations¹¹: time in range 70–180 mg/dl (TIR), in different glucose ranges (time above and below range), mean glucose levels, coefficient of variation (CV), total daily dose (TDD) and bolus proportion. For individuals using Medtronic 780G SmartGuard auto mode, the automated bolus proportion was analyzed as well. The following time periods were compared: 7 and 14 days before and following the first dose of the vaccine; 7 days before and 7 and 14 days following the second dose; 14 days before the first dose and 14 days following the second dose.

Descriptive statistics to ascertain the frequency of side effects was used. The distribution of numerical variables was tested for normality with the Shapiro–Wilk test. Differences between the means of numerical variables pre- and post-vaccination were tested using *T* test for paired samples. All statistical tests were two-sided with a type 1 error set at 5%.

IBM SPSS Statistics v.25 software was used for data analysis.

3 | RESULTS

Characteristics of the study population are presented in Table S1.

3.1 | Glycemic control

Among AHCLs users ($N = 24$, 63% male, mean age 18.4 ± 2.4 years, mean diabetes duration 10.2 ± 4.6 years, mean AHCL duration 6.5 ± 1.5 months, most recent HbA1c mean value $6.5 \pm 0.7\%$, mean BMI 23.4 ± 2.9), 46% were immunized with Pfizer-BioNTech and 54% with Moderna. No significant differences in TIR were observed before and after any dose nor before and after the whole vaccination cycle (Figure 1A). A trend in TIR change close to the first dose was found, so that TIR during the 7 days after the first dose was slightly diminished when compared to TIR in the 7 days before ($71 \pm 13.8\%$ vs. $74 \pm 11.3\%$; p 0.05). Moreover, CV was significantly lower after the whole vaccination cycle (CV pre-vaccination $35.1 \pm 6.9\%$ vs. CV post-vaccination $33.5 \pm 6.3\%$; p 0.031; Figure 1A). No other significant difference was observed in glycemic metrics, TDD or bolus proportion before/after any dose nor before/after the whole vaccination cycle, not even in automated bolus proportion (Medtronic; Figure 1A).

Among isCGM users ($N = 15$, 47% male, mean age 18.3 ± 1.5 years, mean diabetes duration 9.1 ± 4.6 years, most recent HbA1c mean value $7.5 \pm 0.8\%$, mean BMI 21.4 ± 2.3), 33% received the Pfizer- BioNTech vaccine and 67% Moderna. No significant difference in TIR, mean glucose levels, CV, was observed in any of the time periods compared (Figure 1B).

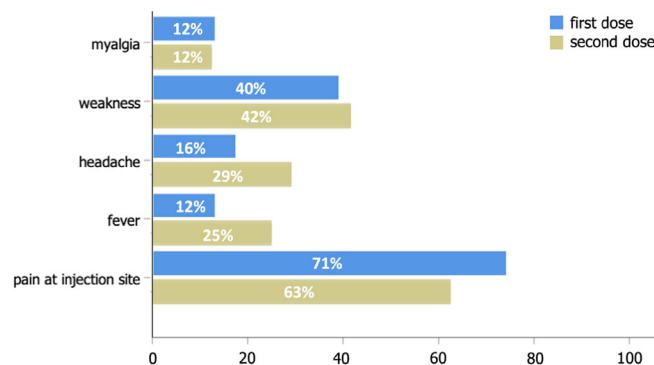


FIGURE 2 Bar chart for adverse effects after the first and second dose of SARS-CoV-2 vaccination. In both cases, the most common adverse reaction was pain at injection site. Some systemic symptoms (fever and headache) were more common after the second dose. No severe adverse reactions were recorded

Considering the sample as a whole CV was confirmed significantly lower after the vaccination cycle (CV pre-vaccination $37.8 \pm 7.9\%$ vs. CV post-vaccination $36 \pm 7.5\%$; p 0.020).

3.2 | Adverse effects

The main complaints after vaccination were pain at injection site (71% after the first, 63% after the second dose), followed by weakness (approximately 40% after both doses), headache (16% after the first, 29% after the second dose), fever (12% after first, 25% after second dose) and myalgia (12% after both doses; Figure 2). No severe adverse reactions, diabetic ketoacidosis (DKA) or severe hypoglycemia (SH) were reported.

4 | DISCUSSION

SARS-CoV-2 vaccination has been prioritized for both T1D and T2D individuals, who carry a worse prognosis, especially if with poor metabolic control, compared to healthy people.⁶ At the time of writing it was recommended for T1D children >12 years as well, even if the infection seems to be mild in pediatric, as recorded in T1D Exchange COVID-19 registry and the role played by age in determining disease severity is crucial.¹²

One of the possible effects of COVID-19 vaccination, however, could be a rise in glycemic levels, due to immune system activation or to stress related to the vaccine itself. To our knowledge this is the first study about the effect of COVID-19 vaccination on glycemic control in youth with T1D, users of technology. No significant difference in glucose control and glycemic metrics was observed at different times of a whole vaccination cycle, regardless of the different technology in use. In subjects treated by AHCLs, this could be determined by the fact that the technology algorithm can compensate a transient increase in glycemic levels caused by the vaccine. However, no changes were observed in TDD, bolus proportion or, when available, in automatic bolus proportion. Interestingly, a significant reduction in CV after the whole vaccination cycle in AHCLs users was found. This

could be explained by the fact that T1D individuals become more experienced in the use of the AHCLs throughout the month between the two doses, or to the self-adjusting nature of the algorithm. No severe reactions nor important/unexpected side effects were reported and systemic symptoms (fever and headache) were more frequently reported after the second dose.

A previously published study showed that glycemic control worsened after COVID-19 vaccination in three T2D adults treated with oral hypoglycemic medications and insulin.¹³ In two cases, hyperglycemia was self-limiting, while in one glucose levels remained high for a month and needed metformin dosage increase.

Similarly, a temporary worsening of glycemic control, lasting 1 week, after COVID-19 vaccine was shown in 20 T1D adults using isCGM, more pronounced in older subjects under oral hypoglycemic medications.¹⁴

Another study did not find significant diabetes control modification after vaccination in 35 adults with autoimmune diabetes using a CGM system (31% closed loop systems, 69% MDI or CSII), however possible increase in insulin requirement was not analyzed.¹⁵

The main limits of our study were the low sample size and the single-center design, but these data can be preliminary for further studies with larger sample size, younger T1D individuals and longer-term follow-up, as we go on with pediatric vaccination for SARS-CoV-2 and its approval for children <12 years. We did not take into consideration separately glycemic control 24–48 hours after vaccination because, even if a perturbation of glucose levels existed, it would be similar to hyperglycemia due to reasons such as other vaccines, intercurrent illness and self-limiting stress hyperglycemia in general.

In conclusion, we found that COVID-19 vaccination is not associated to significant perturbation of glycemic control in adolescents and young adults with T1D, and that, if elevation of glucose values occurs, it is mild, transient, tolerable and not requiring insulin dose adjustment. Side effects are mild and similar to those reported in the general population. All in all, this information could be of clinical use when counseling families in order to reassure them about SARS-CoV-2 vaccination in youth with T1D.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

PEER REVIEW

The peer review history for this article is available at <https://publons.com/publon/10.1111/pedi.13326>.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This paper does not report on primary research (noninterventional study). All data analyzed were collected as part of routine diagnosis and treatment.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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