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Type 1 diabetes, COVID-19 vaccines and short-term safety: Subgroup analysis from the global COVAD study

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ABSTRACT

Aims/Introduction: Coronavirus disease 2019 (COVID-19) vaccinations have been proven to be generally safe in healthy populations. However, the data on vaccine safety in patients with type 1 diabetes are scarce. This study aimed to evaluate the frequency and severity of short-term (<7-day) adverse vaccination events (AEs) and their risk factors among type 1 diabetes patients.

Materials and Methods: This study analyzed data from the COVID-19 vaccination in Autoimmune Diseases (COVAD) survey database (May to December 2021; 110 collaborators, 94 countries), comparing <7-day COVID-19 vaccine AE among type 1 diabetes patients and healthy controls (HCs). Descriptive statistics; propensity score matching (1:4) using the variables age, sex and ethnicity; and multivariate analyses were carried out.

Results: This study analyzed 5,480 completed survey responses. Of all responses, 5,408 were HCs, 72 were type 1 diabetes patients (43 females, 48.0% white European ancestry) and Pfizer was the most administered vaccine (39%). A total of 4,052 (73.9%) respondents had received two vaccine doses. Patients with type 1 diabetes had a comparable risk of injection site pain, minor and major vaccine AEs, as well as associated hospitalizations to HCs. However, type 1 diabetes patients had a higher risk of severe rashes (3% vs 0.4%, OR 8.0, 95% confidence interval 1.7–36), $P = 0.007$), although reassuringly, these were rare ($n = 2$ among type 1 diabetes patients).

Conclusions: COVID-19 vaccination was safe and well tolerated in patients with type 1 diabetes with similar AE profiles compared with HCs, although severe rashes were more common in type 1 diabetes patients.

†The complete list of authors part of the COVAD Study Group as well as their affiliations are provided in Appendix S1S1.

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INTRODUCTION

Patients with diabetes mellitus have been identified as a high-risk group for severe acute respiratory syndrome-associated coronavirus-2 (SARS-CoV-2) infection and poor coronavirus disease 2019 (COVID-19) outcomes. A possible pathophysiological basis might lie in the bidirectional relationship between diabetes and SARS-CoV-2 infection. Poor glycemic control in patients with diabetes might lead to alterations in innate cell-mediated immunity, low leukocyte recruitment, decreased macrocytic phagocytosis and poor cytokine response, which are believed to facilitate the progression of SARS-CoV-2 infection to severe COVID-19[1]. In contrast, the hyperinflammatory state associated with COVID-19 can exacerbate insulin resistance, thus worsening glycemic control[1].

COVID-19-associated mortality is significantly high, especially among black and Asian type 1 diabetes patients, with patients with additional comorbidities, including hypertension and dyslipidemia, at a greater risk[1,2]. In 2020, a study reported that >50% of type 1 diabetes patients with COVID-19 infection developed hyperglycemia; one-third of whom experienced diabetic ketoacidosis[3]. COVID-19 is also believed to accelerate the cardiovascular and renal complications of diabetes[2].

Despite the higher susceptibility to infection and higher risk of COVID-19-associated morbidity and mortality, vaccine hesitancy remains a prevalent problem in patients with type 1 diabetes[4-6]. Isolated anecdotal reports of the rapid development of diabetic ketoacidosis or severe hyperglycemia in type 1 diabetes patients after the administration of messenger ribonucleic acid vaccines have further precipitated this hesitancy[7,8].

The safety and efficacy of COVID-19 vaccines have been extensively studied and reported in the general population. However, substantial gaps remain in vaccine safety data among patients with autoimmune diseases, including type 1 diabetes[9]. This propagates uncertainty, and thus, vaccine hesitancy. Given the increased risks of morbidity and mortality, COVID-19 vaccination might provide an effective recourse to reduce these severe outcomes.

Here, we explore the frequency and severity of COVID-19 vaccine side-effects among type 1 diabetes patients compared with healthy controls (HCs) using data from the COVID-19 vaccination in autoimmune diseases (COVAD) international survey.

MATERIALS AND METHODS

Study design

The COVAD study is a global multicentric patient self-reported e-survey to assess post-COVID-19 vaccination adverse events (AEs) in patients with autoimmune diseases carried out in early 2021[10]. At the time of data collection for this study, the survey questionnaire was disseminated in healthcare centers in 94 countries targeting patients with rheumatic or non-rheumatic autoimmune disorders, as well as healthy controls through social media platforms and patient support groups. The Checklist for Reporting Results of the Internet E-Surveys (CHERRIES) was adhered to for survey design, validation, pilot testing and extensive vetting by experts[11,12].

Data collection

The COVAD study was designed to study different adverse events in patients with different autoimmune diseases. This was a comprehensive dataset involving participants diagnosed with different systemic autoimmune diseases, including type 1 diabetes, inflammatory bowel disease, autoimmune thyroid diseases and the entire spectrum of autoimmune rheumatic diseases. The detailed study protocol is available online in a separate publication[10]. The study questionnaire consisted of 36 questions with a core item set of demographics, autoimmune rheumatic diseases details, COVID-19 infection history and course, vaccination details, 7-day post-vaccination adverse events, and outcome measures using the Patient-Reported Outcomes Measurement Information System (PROMIS) tool[13]. We used the Centers for Disease Control and Prevention website for the major and minor adverse events of COVID vaccines within 7 days of vaccination[14].

A validated questionnaire was hosted on an online platform – surveymonkey.com – following pilot testing and translations, and extensively circulated by the international COVAD study group (110 collaborators, 94 countries) in their clinics, patient support groups and social media platforms. Convenience sampling, snowball and targeted approaches were used to include any interested respondent aged >18 years.

Data extraction

Among the survey respondents, a subgroup of individuals with type 1 diabetes was identified for analysis for this manuscript. Data were extracted from the COVAD study database on 1 January 2022. Respondents who had completed the survey in full and had received at least a single dose of a COVID-19 vaccine were included in the analysis. Out of a total of 18,883 respondents, 10,479 completed the survey. After removing 4,999 respondents with autoimmune rheumatic diseases, 5,408 healthy controls and 72 respondents with type 1 diabetes were identified. Relevant outcome measures: 7-day vaccine AEs, as well as demographic details and the type of COVID-19 vaccine received were retrieved. Vaccine AEs were categorized as minor and major adverse events.

Minor AEs included injection site (arm) pain and soreness, muscle pain in all arms and legs, body ache, fever, chills, nausea/vomiting, diarrhea, headache, rash, fatigue, abdominal pain, high pulse rate or palpitations, rise in blood pressure, fainting, difficulty in breathing, dizziness, chest pain, and other unlisted specified by the respondent as a response to an open-ended question. Major AEs included anaphylaxis (shock), marked difficulty in breathing, tongue swelling or throat closure, severe diffuse body rash (hives), hospitalization and others specified by the respondent.

Ethical considerations

Ethical approval was obtained from the Institutional Ethics Committee of Sanjay Gandhi Postgraduate Institute of Medical Sciences, Raebareli Road, Lucknow, Uttar Pradesh, India, and all participants consented electronically as per local guidelines.

Statistical analysis

Descriptive statistics were carried out, and categorical variables are presented in frequencies (n) and percentages (%). Continuous variables are presented as mean (range). The χ^2-test and Mann–Whitney U-test were used to compare type 1 diabetes patients with HCs for categorical and continuous variables, respectively (Table 1).

To address bias arising out of a small number of type 1 diabetes patients and the multifactorial nature of perceived side-effects, we carried out propensity score matching (PSM). PSM 1:4 match was carried out using the variables age, sex and ethnicity, with a tolerance cut-off of 0 to obtain a matched population for type 1 diabetes patients from the cohort of HCs.

Although PSM is a robust analysis method, it cannot control for the unmeasured confounding, and causes a reduction in sample size, because matches for all patients cannot be found, whereas multivariate regression allows balances of all covariates[15]. Hence, results were further compared using logistic regression. Binary logistic regression adjusted for age, sex, ethnicity and stratified by country of origin was also carried out between type 1 diabetes patients and HCs for the vaccine-related AEs. A P-value <0.05 was considered statistically significant. Statistics were carried out using IBM SPSS version 28 (IBM, Armonk, NY, USA).

RESULTS

Population characteristics

Among 18,883 respondents to the survey at the time of data extraction, those with autoimmune disorders other than type 1 diabetes were excluded. Of these, 5,408 HCs and 72 type 1 diabetes patients were included in the final analysis (Figure 1), with baseline characteristics detailed as Table 1. All respondents included in the final analysis had received at least a single dose of the vaccine at the time of survey completion, and 73.9% had received two primary doses. Most respondents among HCs (36%, n = 1937) and type 1 diabetes patients (39%, n = 28) had received the Pfizer vaccine ($P < 0.001$).

Propensity score matching analysis

A total of 72 type 1 diabetes patients and 280 HCs were PSM matched by the covariates mentioned prior (Table 2). Patients with type 1 diabetes had a higher frequency of the minor AEs of fever (odds ratio [OR 2.0], 95% confidence interval [CI] 1.1–4.0; P = 0.023), diarrhea (OR 5.4, 95% CI 1.1–24.8; P = 0.015)

Table 1 | Population characteristics of the whole unmatched cohort

Variable	Total (n = 5,480)	Type 1 diabetes patients (n = 72)	HCs (n = 5,408)	P-value
Mean age, years (range)	35 (26–48)	45 (34–56)	35 (26–48)	<0.001*
Sex (M : F)	1,830:3,616 (1:1.9)	29:43 (1:1.5)	1,801:3,573 (1:2)	0.227
Ethnicity				
White	2,431 (44)	35 (48)	2,396 (44)	0.147
African American/African origin	36 (0.7)	0 (0)	36 (0.7)	
Asian	1,473 (27)	27 (37)	1,446 (27)	
Hispanic	836 (15)	5 (7)	836 (15)	
Native American/Indigenous/Pacific Islander	29 (0.5)	0 (0)	29 (0.5)	
Do not wish to disclose	369 (6.7)	2 (3)	367 (7)	
Other	301 (5.5)	3 (4)	298 (5.5)	
Vaccine taken				
Pfizer-BioNTech	1965 (36)	28 (39)	1937 (36)	<0.001*
Oxford/AstraZeneca	571 (10)	6 (8)	565 (10)	
Johnson & Johnson (J&J)	46 (0.8)	2 (3)	44 (1)	
Moderna	247 (4.5)	1 (1.4)	246 (4.5)	
Novavax	3 (0.1)	1 (1.4)	2 (0)	
Covishield (serum institute India)	731 (13)	21 (29)	710 (13)	
Covaxin (Bharat Biotech)	130 (2.4)	1 (1.4)	129 (2.4)	
Sputnik	147 (2.7)	2 (3)	145 (2.7)	
Sinopharm	1,308 (24)	7 (10)	1,301 (24)	
I am not sure	36 (0.7)	1 (1.4)	35 (0.6)	
Others	294 (4.4)	2 (3)	294 (5.4)	

The χ^2-test and Mann–Whitney U-test were carried out.
*$P < 0.05$ significant.
F, female; HCs, healthy controls; M, male.

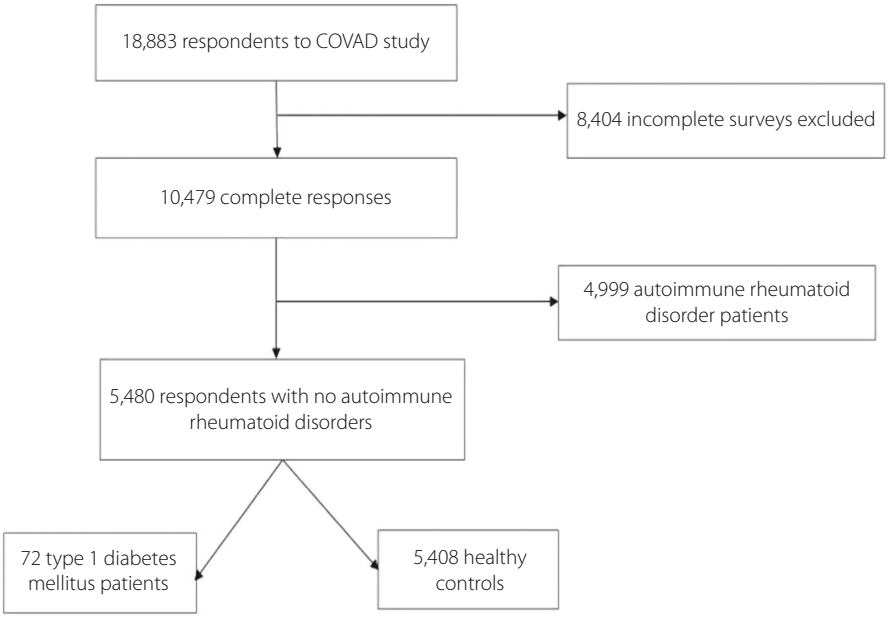

Figure 1 | Flowchart of study participants. COVAD, COVID-19 Vaccination in Autoimmune Diseases.

Table 2 | Population characteristics of the matched cohort (1:4).

Variable	Total (n = 352)	Type 1 diabetes patients (n = 72)	HCs (n = 280)	P-value
Age (years)	44 (34–55)	45 (34–56)	47 (34–56)	0.662
Sex (M : F)	132:220 (1:1.6)	29:43 (1:1.5)	103:177 (1:1.7)	0.585
Ethnicity, n (%)				
African American or of African origin	–	–	–	0.970
Asian	137 (38.9)	27 (37.5)	110 (39.3)	
Caucasian	159 (45.2)	35 (48.6)	124 (44.3)	
Hispanic	31 (8.8)	5 (6.9)	26 (9.3)	
Native American/Indigenous/Pacific Islander	1 (0.3)	0 (0)	1 (0.4)	
Do not wish to disclose (4)	10 (2.8)	2. (2.8)	8 (2.9)	
Other	14 (4.0)	3 (4.2)	11 (3.9)	
Vaccine taken				
Pfizer-BioNTech	113 (32.1)	28 (38.9)	85 (75.2)	<0.001
Oxford/AstraZeneca	22 (6.3)	6 (8.3)	16 (5.7)	
Johnson & Johnson (J&J)	2 (0.6)	0 (0)	2 (2.8)	
Moderna	6 (1.7)	1 (1.4)	5 (1.8)	
Novavax	1 (0.3)	0 (0)	1 (1.4)	
Covishield (serum institute India)	38 (10.8)	21 (29.2)	17 (6.1)	
Covaxin (Bharat Biotech)	4 (1.1)	1 (1.4)	3 (1.1)	
Sputnik	48 (13.6)	2 (9.7)	46 (34.6)	
Sinopharm	104 (29.5)	7 (9.7)	97 (34.6)	
I am not sure	3 (0.9)	1 (1.4)	3 (1.1)	
Others	11 (3.1)	2 (2.8)	9 (3.2)	

Propensity score matching (1:4) carried out with age, sex and ethnicity with tolerance cut-off of 0.1. Eight of the type 1 diabetes patients had only three appropriate matches. F, female; HCs, healthy controls; M, male.

and dizziness (OR 3.5, 95% CI 1.1–10.9; $P = 0.019$) after vaccination compared with matched HCs. However, overall minor AEs, major AEs and hospitalization frequency were reassuringly comparable between the two groups (all $P > 0.05$; Table 3).

Logistic regression analysis

Nearly three-quarters (76%) of type 1 diabetes patients and HCs (77%) reported some form of vaccine AEs, including both minor and major AEs (OR 0.9, 95% CI 0.5–1.6; $P = 0.868$), with injection site pain being the most reported event. The patient-reported frequency of injection site pain was lower in type 1 diabetes patients as compared with HCs, although the significance was lost in the adjusted analysis (Table 4). However, patients with type 1 diabetes had a significantly higher risk of severe rash (diffuse body rash or hives) than HCs (OR 8.0, 95% CI 1.7–36.0; $P = 0.007$), possibly arising out of bias due to limited numbers ($n = 2$). These included a 67-year-old white woman from Australia who received ChAdOx1-S (recombinant) vaccine and a 58-year-old Hispanic man from Mexico who received Ad5-nCoV (CanSino) vaccine. Both these patients reassuringly reported no other complications.

Table 3 | Comparison of vaccine adverse events between type 1 diabetes and healthy controls of the matched cohort: results from propensity score matching analysis

	Type 1 diabetes patients ($n = 72$)	HCs ($n = 280$)	OR (95% CI)	*P*-value
	n (%)	*n* (%)		
Any AE	54 (75.0)	203 (72.5)	–	0.670
Injection site pain	37 (51.4)	139 (49.6)	–	0.792
Minor adverse reaction to vaccine				
Any minor AE	54 (75.0)	203 (72.5)	–	0.670
Myalgia	9 (12.5)	37 (80.4)	–	0.873
Body ache	12 (16.7)	40 (14.3)	–	0.612
Fever	17 (23.6)	36 (12.9)	2.0 (1.1–4.0)	0.023
Chills	8 (11.1)	20 (7.1)	–	0.267
Nausea and vomiting	5 (6.9)	9 (3.2)	–	0.149
Headache	13 (18.1)	51 (18.2)	–	0.975
Rashes	1 (1.4)	3 (1.1)	–	0.821
Fatigue	17 (23.6)	63 (22.5)	–	0.841
Diarrhea	4 (5.6)	3 (1.1)	5.4 (1.1–24.8)	0.015
Abdominal pain	1 (1.4)	2 (0.7)	–	0.579
Rise in blood pressure	0 (0)	1 (0.4)	–	0.612
Difficulty in breathing	1 (1.4)	2 (0.7)	–	0.579
Dizziness	6 (8.3)	7 (2.5)	3.5 (1.1–10.9)	0.019
Chest pain	1 (1.4)	3 (1.1)	–	0.821
Others	2 (2.7)	19 (6.7)	–	0.299
Major AEs				
Any major AEs	2 (2.8)	7 (2.5)	–	0.894
Anaphylaxis	0 (0)	0 (0)	–	–
Marked difficulty in breathing	1 (1.4)	3 (1.1)	–	0.821
Throat closure	0 (0)	0 (0)	–	–
Severe rashes	2 (4)	2 (0.7)	–	0.141
Others	0 (0)	0 (0)	–	–
Hospitalization	1 (1.4)	1 (0.4)	–	0.299

AE, adverse effect; CI, confidence interval; HC, healthy control; OR, odds ratio.

DISCUSSION

COVID-19 has been a significant cause of global morbidity and mortality[14]. People with chronic diseases, including diabetes, represent a high-risk group for poor COVID-19 outcomes, including an increased risk of long COVID-19 or post-COVID-19 syndrome, myocardial infarction and cerebrovascular accidents[16-19]. Achieving global vaccination and reducing vaccine hesitancy is a priority for these individuals[20,21]. Unfortunately, safety data on adults living with type 1 diabetes are limited, and most studies are physician reported, whereas patient-reported data are lacking in the literature[16].

We reassuringly found a high rate of vaccine uptake among patients with type 1 diabetes, and a favorable vaccine safety profile comparable with HCs, except for a higher frequency of fever, diarrhea and dizziness, with the majority of reported AEs being minor and not requiring hospitalization, mirroring previous studies[10,22]. The results of logistic regression did show a significantly increased risk for severe rashes in type 1 diabetes patients as compared with HCs, but the absolute number of type 1 diabetes patients reporting severe rash was only two. These findings were also consistent with that of other systemic autoimmune diseases[9,23].

Despite data on COVID-19 vaccine side-effects in type 1 diabetes patients, reports of severe vaccine AEs are scarce and anecdotal[7,20]. Furthermore, in most of these cases, the onset of hyperglycemic symptoms was 15 h to 6 days post-vaccination, raising the possibility that these post-vaccination hyperglycemic episodes were likely immune-mediated[20]. The possible role of adjuvants in inducing aberrant immune responses in these patients with altered immune status cannot be excluded[24]. A few cases of diabetic ketoacidosis and hyperosmolar hyperglycemic state have been reported among type 2 diabetes patients with glycated hemoglobin >12%[25,26], indicating poor glycemic control. Therefore, the addition of oxidative stress from vaccinations to poor glycemic control might be associated with post-vaccination complications[20]. The isolated reports should not deter COVID-19 vaccination in this patient group. Furthermore, a recent study showed the overall short-term safety of SARS-CoV-2 vaccination on glycemic control in autoimmune diabetes patients[27].

The limitations of the present study include the self-reported nature of AEs, which could not be verified, with a relatively small number of type 1 diabetes patients despite a large control group. We did not assess glycemic control. The survey did not

Table 4 | Comparison of vaccine adverse events between type1 diabetes patients and healthy controls of unmatched cohort (univariate and multivariate)

	Type 1 diabetes patients (n = 72)	HCs (n = 5,408)	Univariate		Multivariate[†]	
	n (%)	n (%)	OR (CI)	P-value	OR (CI)	P-value
Any AE	55 (76)	4,176 (77)	0.9 (0.5–1.6)	0.868		
Injection site pain	37 (51)	3,401 (63)	0.6 (0.3–0.9)	0.045*	0.6 (0.4–1.1)	0.113
Minor AEs to vaccine						
Any minor AE	54 (75)	4,175 (77)	0.8 (0.5–1.5)	0.659		
Myalgia	9 (12)	829 (15)	0.7 (0.3–1.5)	0.508		
Body ache	12 (16)	1,149 (21)	0.7 (0.3–1.3)	0.345		
Fever	17 (23)	1,050 (19)	1.2 (0.7–2.2)	0.372		
Chills	8 (11)	694 (13)	0.8 (0.4–1.7)	0.664		
Nausea and vomiting	5 (7)	256 (5)	1.5 (0.6–3.7)	0.382		
Headache	13 (18)	1,266 (23)	0.7 (0.3–1.3)	0.286		
Rashes	1 (1.4)	64 (1)	1.1 (0.1–8.5)	0.873		
Fatigue	17 (23)	1,491 (27)	0.8 (0.4–1.4)	0.455		
Diarrhea	4 (5)	132 (2)	2.3 (0.8–6.5)	0.091		
Abdominal pain	1 (1.4)	83 (1.5)	0.9 (0.1–6.5)	0.920		
Rise in pulse rate	0 (0)	143 (3)	–	0.162		
Rise in blood pressure	0 (0)	51 (1)	–	0.408		
Fainting	0 (0)	22 (0.5)	–	0.588		
Difficulty in breathing	1 (1.4)	65 (1)	1.9 (0.8–4.5)	0.885		
Dizziness	6 (8)	242 (4)	1.9 (0.8–4.5)	0.118		
Chest pain	1 (1.4)	69 (1)	1.0 (0.1–7.9)	0.932		
Others	2 (3)	354 (6)	0.4 (0.1–1.6)	0.212		
Major AEs						
Any major AEs	2 (3)	128 (2)	1.1 (0.2–4.8)	0.820		
Anaphylaxis	0 (0)	5 (0.1)	–	0.796		
Marked difficulty in breathing	1 (1.4)	34 (0.6)	2.2 (0.3–16.4)	0.421		
Throat closure	0 (0)	9 (0.2)	–	0.729		
Severe rashes	2 (3)	20 (0.4)	7.6 (1.7–33.5)	0.001*	7.4 (1.6–33.8)	0.009*
Others	0 (0)	88 (1.6)	–	0.536		
Hospitalization	1 (1.4)	12 (0.2)	6.3 (0.8–49.3)	0.158		

AE, adverse effect; CI, confidence interval; HCs, healthy controls; OR, odds ratio. *Statistically significant. [†]Binary logistic regression adjusted for age, gender, ethnicity, vaccine type and stratified by country of origin.

collect data on other comorbidities, especially type 2 diabetes. The COVAD survey was designed to outline patient experience and embody patient voice; therefore, complications, such as type 1 diabetes-related ketoacidosis and other laboratory-based AEs, were omitted from the survey questionnaire. Due to the small cohort of type 1 diabetes patients, the differences in AEs among different vaccine categories were not analyzed. We recommend that the identification of AEs in specific vaccine groups might be a focused area of interest in future studies. A follow-up study addressing these lacunae is underway in the form of a second COVAD survey[24].

A plethora of studies related to physician-reported vaccine AEs; however, a substantial gap exists between physician-defined AEs and what the patient experiences as an AE, which could potentially contribute to continued vaccine hesitancy. It is crucial to bridge this gap and identify the patient's experience of vaccine AEs.

Nevertheless, the present study provides unique sights into the effects of COVID-19 vaccination in this rare and understudied disease, with a geographically and ethnically diverse global sample of patients, giving generalizability and reliability to our findings, and might aid physicians in making informed decisions regarding vaccination in these patients.

The present study reiterates that COVID vaccination is safe in adults living with type 1 diabetes, and adds to the growing body of evidence that the benefits of COVID-19 vaccination in reducing severe COVID-19 outcomes outweigh the risk of small potential AEs in patients with chronic diseases, such as type 1 diabetes.

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DISCLOSURE

ALT has received honoraria for advisory boards and speaking for Abbvie, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB. IP has received research funding and/or honoraria from Amgen, AstraZeneca, Aurinia Pharmaceuticals, Elli Lilly and Company, Gilead Sciences, GlaxoSmithKline, Janssen Pharmaceuticals, Novartis, and F. Hoffmann-La Roche AG. RA has a consultancy relationship with and/or has received research funding from Bristol Myers-Squibb, Pfizer, Genentech, Octapharma, CSL Behring, Mallinckrodt, AstraZeneca, Corbus, Kezar, Abbvie, Janssen, Kyverna Alexion, Argenx, Q32, EMD-Serono, Boehringer Ingelheim, Roivant, Merck, Galapagos, Actigraph, Scipher, Horizon Therepeutics, Teva, Beigene, ANI Pharmaceuticals, Biogen, Nuvig, Capella Bioscience, and CabalettaBio. TV has received speaker honoraria from Pfizer and AstraZeneca. The other authors declare no conflict of interest.

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No part of this manuscript is copied or published elsewhere in whole or in part.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are not publicly available, but are available from the corresponding author upon reasonable request.

REFERENCES

1. Ahmed AS, Alotaibi WS, Aldubayan MA, *et al*. Factors affecting the incidence, progression, and severity of COVID-19 in type 1 diabetes mellitus. *Biomed Res Int* 2021; 2021: 1676914.
2. Holman N, Knighton P, Kar P, *et al*. Risk factor or COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study. *Lancet Diabetes Endocrinol* 2020; 8: 823–833.
3. Ebekozien OA, Noor N, Gallagher MP, *et al*. Type 1 diabetes and COVID-19: preliminary findings from a multicenter surveillance study in the U.S. *Diabetes Care* 2020; 43: e83–e85.
4. Wang Y, Duan L, Li M, *et al*. COVID-19 vaccine hesitancy and associated factors among diabetes patients: a cross-sectional survey in Changzhi, Shanxi, China. *Vaccines* 2022; 10: 129.
5. Aldossari KK, Alharbi MB, Alkahtani SM, *et al*. COVID-19 vaccine hesitancy among patients with diabetes in Saudi Arabia. *Diabetes Metab Syndr* 2021; 15: 102271.
6. Scoccimarro D, Panichi L, Ragghianti B, *et al*. Sars-CoV2 vaccine hesitancy in Italy: a survey on subjects with diabetes. *Nutr Metab Cardiovasc Dis* 2021; 31: 3243–3246.
7. Zilbermint M, Demidowich AP. Severe diabetic ketoacidosis after the second dose of mRNA-1273 COVID-19 vaccine. *J Diabetes Sci Technol* 2022; 16: 248–249.

8. Wilson C. Vaccine side effects. *New Sci* 2021; 250: 10.
9. Gil-Vila A, Ravichandran N, Selva-O'Callaghan A, *et al*. COVID-19 vaccination in autoimmune diseases (COVAD) study: vaccine safety in idiopathic inflammatory myopathies. *Muscle Nerve* 2022; 66: 426–437.
10. Sen P, Gupta L, Lilleker JB, *et al*. COVID-19 vaccination in autoimmune disease (COVAD) survey protocol. *Rheumatol Int* 2022; 42: 23–29.
11. Eysenbach G. Improving the quality of web surveys: the checklist for reporting results of internet E-surveys (CHERRIES). *J Med Internet Res* 2004; 6: e34.
12. Gaur PS, Zimba O, Agarwal V, *et al*. Reporting survey based studies – a primer for authors. *J Korean Med Sci* 2020; 35: 1–15.
13. PROMIS, n.d. Available from: https://www.healthmeasures.net/score-and-interpret/interpret-scores/promis Accessed October 20, 2022.
14. US Centers for Disease Control and Prevention. Possible side effects after getting a COVID-19 vaccine. Published September 28, 2021. Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/expect/after.html Accessed September 29, 2021.
15. Benedetto U, Head SJ, Angelini GD, *et al*. Statistical primer: propensity score matching and its alternatives. *Eur J Cardiothorac Surg* 2018; 53: 1112–1117.
16. Meo SA, Bukhari IA, Akram J, *et al*. COVID-19 vaccines: comparison of biological, pharmacological characteristics and adverse effects of Pfizer/BioNTech and Moderna vaccines. *Eur Rev Med Pharmacol Sci* 2021; 25: 1663–1669.
17. Modin D, Claggett B, Køber L, *et al*. Influenza vaccination is associated with reduced cardiovascular mortality in adults with diabetes: a nationwide cohort study. *Diabetes Care* 2020; 43: 2226–2233.
18. Gomez CAG, Cosatti M, Coello VVC, *et al*. Ab1101 prevalence of long covid in rheumatic disease patients: analysis of SAR covid registry. *Ann Rheum Dis* 2022; 81: 1668–1669.
19. Dilorio M, Kennedy K, Liew JW, *et al*. Prolonged COVID-19 symptom duration in people with systemic autoimmune rheumatic diseases: results from the COVID-19 global rheumatology alliance vaccine survey. *RMD Open* 2022; 8: e002587.
20. Ganakumar V, Jethwani P, Roy A, *et al*. Diabetic ketoacidosis (DKA) in type 1 diabetes mellitus (T1DM) temporally related to COVID-19 vaccination. *Diabetes Metab Syndr Clin Res Rev* 2022; 16: 102371.
21. Singh A, Khillan R, Mishra Y, *et al*. The safety profile of COVID-19 vaccinations in the United States. *Am J Infect Control* 2022; 50: 15–19.
22. Dicembrini I, Vitale V, Cosentino C, *et al*. Interstitial glucose monitoring, type 1 diabetes and COVID-19 vaccine: the patient-reported outcomes and vaccine-associated changes in glucose and side effects (PRO-VACS). *Acta Diabetol* 2022; 59: 435–438.
23. Sen P, Ravichandran N, Nune A, *et al*. COVID-19 vaccination-related adverse events among autoimmune disease patients: results from the COVAD study. *Rheumatology (Oxford)* 2022; 62: 65–76.
24. Fazal ZZ, Sen P, Joshi M, *et al*. COVAD survey 2 long-term outcomes: unmet need and protocol. *Rheumatol Int* 2022; 42: 1–8.
25. Edwards AE, Vathenen R, Henson SM, *et al*. Acute hyperglycaemic crisis after vaccination against COVID-19: a case series. *Diabet Med* 2021; 38: e14631.
26. Lee HJ, Sajan A, Tomer Y. Hyperglycemic emergencies associated with COVID-19 vaccination: a case series and discussion. *J Endocr Soc* 2021; 5: bvab141.
27. D'Onofrio L, Coraggio L, Zurru A, *et al*. Short-term safety profile of Sars-Cov2 vaccination on glucose control: continuous glucose monitoring data in people with autoimmune diabetes. *Diabetes Res Clin Pract* 2021; 179: 109022.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1 | COVID-19 Vaccination in Autoimmune Diseases (COVAD) Study Group Author List and Affiliations.