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Research Letter

Is vaccination against COVID-19 associated with psoriasis or eczema flare? Self-controlled case series analysis using data from the Clinical Practice Research Datalink (Aurum)

Dear Editor, Case reports and uncontrolled case series have reported psoriasis and eczema flares following COVID-19 vaccination,[1–3] lending credence to the idea that vaccination could trigger disease flares. Up to 54% of vaccine-hesitant patients with psoriasis cite apprehension of disease flare as their primary reason for vaccine hesitancy.[4–6] To the best of our knowledge, no adequately controlled study has assessed the association between COVID-19 vaccination and skin disease flare. We investigated the risk of flare of psoriasis or eczema following COVID-19 vaccination using data from the Clinical Practice Research Datalink (CPRD) Aurum. CPRD is a longitudinal anonymized electronic database of health records from 19 million patients in the UK[7] and includes information on demographic and lifestyle factors, diagnoses, primary-care prescriptions and vaccinations.

This study was approved by CPRD Research Data Governance (reference: 21_000670). This study used data from the CPRD. Due to the CPRD data sharing policy, we are unable to share this study's data. However, access to CPRD data can be directly requested from the CPRD.

Self-controlled case series analysis was used in this study. This analytical method uses data from exposed participants who also develop an outcome, and accounts for between-person confounding.[8] It is extensively used in vaccine safety studies.

Inclusion criteria were adults aged ≥ 18 years, with at least one primary-care consultation for atopic dermatitis/eczema or psoriasis, with or without arthritis, who received at least one primary-care prescription of conventional immunesuppressing treatments, provided they also received at least one vaccination against COVID-19 *and* consulted their general practitioner for at least one skin flare between 1 December 2020 and 31 December 2021. Vaccination and vaccine brand were defined using product codes and vaccination dates. COVID-19 was defined using either general practitioner diagnosis or test results recorded in the CPRD.

Skin disease flare was defined as primary-care consultation with diagnostic coding for atopic dermatitis/eczema or cutaneous psoriasis and prescription of drug(s) used for skin disease flare on the same or subsequent date without prescription of the qualifying drug in the preceding 90 days. This minimized the possibility of routine consultations and repeat prescriptions being defined as disease flare. Date of primary-care consultation was the outcome date. Participants contributed data from multiple flares; however, consultations within 14 days were considered part of the same flare.

The study period (1 December 2020 to 31 December 2021) was divided into 21 days vaccine exposed, 7 days prevaccination and the remaining vaccine-unexposed periods. The vaccine-exposed period was 21 days postvaccination as it takes approximately 1–2 weeks for COVID-19 immunization to induce an immunological response. We hypothesized that this period of immune reconstitution was most likely to be associated with increased disease activity. As patients with disease flare may delay vaccination, the 7 days preceding vaccination were considered separate from the vaccine-unexposed period to minimize potential reverse causation.

A Poisson model conditioned on the number of events and adjusted for seasons was fitted to calculate the adjusted incidence rate ratio and 95% confidence interval for the association between vaccination and skin flares. Stratified analysis considered different vaccine doses, technology of first vaccine received and type of skin disease. COVID-19 infection before the first vaccination had follow-up censored at the second dose. Data were analysed using Stata v.16 (StataCorp LLC, College Station, TX, USA). A two-sided $P < 0{\cdot}05$ was considered statistically significant.

Data for 1963 patients were included, with 1770 (90·2%), 178 (9·1%) and 15 (0·8%) patients having had one, two and three skin disease flares, respectively. Their mean (SD) age was 50 (17) years, 1126 (57·4%) were women, 1154 (58·8%) had psoriasis and 809 (41·2%) had eczema. Overall, 42% were prescribed immune-suppressing drugs within the 13-month study period. With regard to vaccination, 1062 (54·1%), 799 (40·7%) and 102 (5·2%) patients received three, two and one vaccinations against COVID-19, respectively.

Vaccination against COVID-19 was not associated with skin disease flares in the vaccine-exposed period (Table 1). The rate ratios for skin disease flare in the vaccination-exposed period were similar in those with psoriasis or eczema, in those receiving or not receiving immunosuppression during the study period, and in those vaccinated with mRNA-BNT162b2 or AZD1222. The rate ratio of skin disease flare in the 21 days after vaccination with the first dose of COVID-19 vaccine was *lower* among patients with previous COVID-19, with an adjusted incidence rate ratio of 0·31 (95% confidence interval 0·10–0·99).

Strengths of this study include use of a nationwide database, an outcome definition that required consultation and flare-treatment prescription on the same or next date and adjustment for season. Limitations include lack of data on self- or hospital-managed flares, flares that did not require treatment change and biologic treatments. However, these factors are unlikely to introduce a differential bias between the exposed and unexposed periods.

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Table 1 The association between COVID-19 vaccination and skin disease flare

	Risk period (days)	Events (*n*)	IRR (95% CI)	Adjusted[a] IRR (95% CI)	*P*-value[a]
All doses	Baseline	1738	1	1	
	7 days before vaccination	114	1·13 (0·93–1·37)	1·11 (0·92–1·34)	0·29
	21 days after vaccination	284	0·97 (0·85–1·10)	0·96 (0·84–1·09)	0·52
Dose number	Baseline	1738	1	1	
1	7 days before vaccination	52	1·28 (0·97–1·68)	1·22 (0·93–1·62)	0·16
1	21 days after vaccination	134	1·10 (0·92–1·31)	1·05 (0·88–1·26)	0·61
2	7 days before vaccination	39	1·02 (0·74–1·40)	0·98 (0·71–1·35)	0·89
2	21 days after vaccination	103	0·90 (0·74–1·40)	0·90 (0·72–1·11)	0·33
3	7 days before vaccination	23	1·05 (0·69–1·59)	1·12 (0·74–1·70)	0·59
3	21 days after vaccination	47	0·82 (0·61–1·10)	0·85 (0·63–1·14)	0·28
Skin disease type					
Eczema	Baseline	737	1	1	
	7 days before vaccination	44	1·05 (0·78–1·43)	1·04 (0·76–1·41)	0·83
	21 days after vaccination	117	0·96 (0·79–1·17)	0·95 (0·78–1·17)	0·66
Psoriasis	Baseline	1001	1	1	
	7 days before vaccination	70	1·18 (0·93–1·51)	1·16 (0·91–1·48)	0·23
	21 days after vaccination	167	0·97 (0·83–1·15)	0·96 (0·80–1·14)	0·61
Prescribed systemic immunosuppressive drugs in the study period					
No	Baseline	1020	1	1	
	7 days before vaccination	67	1·15 (0·90–1·48)	1·15 (0·90–1·48)	0·27
	21 days after vaccination	170	1·01 (0·85–1·18)	1·01 (0·85–1·20)	0·88
Yes	Baseline	718	1	1	
	7 days before vaccination	47	1·10 (0·82–1·48)	1·06 (0·78–1·42)	0·72
	21 days after vaccination	114	0·91 (0·75–1·12)	0·88 (0·72–1·09)	0·24
Vaccine type[b,c]					
m-RNA-BNT162b2	Baseline	412	1	1	
	7 days before vaccination	20	1·05 (0·67–1·65)	1·02 (0·64–1·61)	0·94
	21 days after vaccination	49	0·86 (0·64–1·16)	0·87 (0·64–1·18)	0·36
Vectored DNA (AZD1222)	Baseline	537	1	1	
	7 days before vaccination	31	1·17 (0·82–1·69)	1·15 (0·79–1·65)	0·47
	21 days after vaccination	84	1·06 (0·84–1·34)	1·06 (0·84–1·33)	0·64

CI, confidence interval; IRR, incidence rate ratio. [a]Adjusted for four seasons. [b]First vaccine analysed. [c]People vaccinated with mRNA-1273 vaccine ($n=30$) were excluded from this analysis. Sixty-eight patients (3·5%) did not contribute data for the entire follow-up period due to death ($n=11$) or transfer out of general practice ($n=57$).

Patients with psoriasis or eczema do not have an increased risk of flare of their skin disease following COVID-19 vaccination. This study provides new evidence that will permit healthcare professionals to reassure patients regarding the safety of COVID-19 vaccination with respect to disease stability.

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