Clinical Rheumatology (2022) 41:2257–2260
https://doi.org/10.1007/s10067-022-06081-7

LETTERS OF BIOMEDICAL AND CLINICAL RESEARCH

COVID-19 vaccination outcomes among patients with dermatomyositis: a multicentered analysis

Haig Pakhchanian[1] · Ahmad Saud[2] · Rahul Raiker[3] · Sinan Kardes[4] · Rohit Aggarwal[5] · Latika Gupta[6]

Received: 7 December 2021 / Revised: 21 January 2022 / Accepted: 24 January 2022 / Published online: 27 January 2022

The BNT162b2, mRNA-1273, and Ad26.COV.2.S are the three vaccines that have been instrumental in managing the COVID-19 pandemic in the USA. Despite these vaccines being granted Emergency-Use Authorization by the FDA, safety and efficacy are unclear among autoimmune rheumatic disease patients as these populations were excluded from clinical trials [1–3]. Speculations have been rife that vaccines may trigger autoimmunity, contributing to vaccine hesitancy among those with autoimmune rheumatic disorders such as dermatomyositis (DM) [4]. Therefore, the goal was to evaluate the safety and effectiveness of COVID-19 vaccination among DM patients when compared to vaccinated controls using data from a federated database.

TriNetX (Cambridge, MA) is a multicenter research database that was used in this retrospective cohort study. Validated ICD-10 diagnostic codes and CPT codes were utilized to identify vaccinated patients with and without DM. Inclusion of DM patients was based on a diagnosis of ≥ 1 ICD-10 codes at least 1 year apart. 1:1 propensity score matching (PSM) was then utilized to balance the two cohorts by demographics and comorbidities. Lastly, 1-day anaphylaxis along with 30- and 60-day adverse events of special interest (AESI) as defined by the CDC, breakthrough infection (BI), and all-cause hospitalization (ACH) were assessed using adjusted risk ratios and 95% confidence intervals. To protect the patient health information, TriNetX obfuscates aggregate patient counts ≤ 10 to prevent statistical analysis. Further details regarding this methodology are detailed in previous studies and in the supplement [5].

Before PSM, 1,022,471 vaccinated individuals made up non-DM controls and were compared to 6104 vaccinated DM patients. On average, vaccinated DM patients were composed of older and comorbid patients with higher female and Black representation (Table 1). After PSM, two balanced cohorts of 6103 patients were compared to each another. DM patients did not have a difference in risk for immediate anaphylaxis at 1-day post-immunization (RR: 1.8 (CI: 0.96–3.38), $p = 0.06$), while absolute risk was minimal for DM patients (0.4%). At 30 days post-vaccination, vaccinated DM patients did not experience a difference in risk for AESI, BI, or ACH compared to the control population. However, at 60 days post-vaccination, the DM group had a greater risk for AESI compared to controls (RR: 1.96 (CI: 1.06–3.61), $p = 0.028$) with a small absolute risk of 0.6%. No differences in risk for BI and ACH were observed 60 days post-vaccination (Table 2). DMARD and glucocorticoid use did not impact AESI, BI, or ACH at any time interval. Among the three administered vaccines, BI was greater among BNT162b2 (0.9% vs. 0.5%, p-0.026) though this was also the most common vaccine administered (4411/6104).

Widespread efforts to vaccinate the public in attempts to achieve herd immunity makes it increasingly vital for rheumatologists to have an evidence base by which to address patient queries and avoid misinformation, especially surrounding the issue of immunosuppression [6, 7]. We observed a small absolute risk in DM patients;

Haig Pakhchanian and Ahmad Saud contributed equally to this work.

✉ Latika Gupta
drlatikagupta@gmail.com

Sinan Kardes
sinan.kardes@istanbul.edu.tr

1 George Washington University School of Medicine and Health Sciences, Washington, DC, USA

2 Department of Medicine, Royal College of Surgeons Ireland, Dublin, Ireland

3 West Virginia University School of Medicine, Morgantown, WV, USA

4 Department of Medical Ecology and Hydroclimatology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

5 Department of Medicine, University of Pittsburgh, Pittsburgh, PA, USA

6 Department of Rheumatology, Royal Wolverhampton Hospitals NHS Trust, Wolverhampton WV10 0QP, UK

Table 1 Baseline characteristics of the dermatomyositis and non-inflammatory myositis patient cohorts before and after propensity matching

Characteristic name	Before propensity matching			After propensity matching		
	Vaccinated DM ($N=6104$)	Vaccinated non-DM ($N=1,022,471$)	Standard mean difference	Vaccinated DM ($N=6103$)	Vaccinated non-DM ($N=6103$)	Standard mean difference
BMI, kg/m^2	30.33 ± 7.54	28.88 ± 6.69	0.20	30.33 ± 7.54	30.94 ± 7.47	0.08
Age, years	62.31 ± 13.49	54.36 ± 18.61	0.49	62.3 ± 13.49	62.3 ± 13.49	0.06
Female	4880 (79.95%)	574,288 (56.17%)	0.53	4879 (79.94%)	4846 (79.40%)	0.01
White	4273 (70.00%)	669,741 (65.50%)	0.10	4272 (70.00%)	4335 (71.03%)	0.02
Black or African American	1287 (21.09%)	146,387 (14.32%)	0.18	1287 (21.09%)	1280 (20.97%)	0.03
Neoplasms	4608 (75.49%)	196,699 (19.24%)	1.36	4607 (75.49%)	4635 (75.95%)	0.01
Essential (primary) hypertension	4482 (73.43%)	253,824 (24.83%)	1.11	4481 (73.42%)	4537 (74.34%)	0.02
Chronic lower respiratory diseases	3233 (52.97%)	100,743 (9.85%)	1.05	3232 (52.96%)	3252 (53.29%)	0.01
Diabetes mellitus	2184 (35.78%)	102,052 (9.98%)	0.65	2183 (35.77%)	2202 (36.08%)	0.01
Ischemic heart diseases	1912 (31.32%)	76,153 (7.45%)	0.63	1911 (31.31%)	1931 (31.64%)	0.01
Nicotine dependence	1374 (22.51%)	44,831 (4.39%)	0.55	1373 (22.50%)	1330 (21.79%)	0.02
Chronic kidney disease	1243 (20.36%)	44,633 (4.37%)	0.50	1242 (20.35%)	1158 (18.97%)	0.04
Heart failure	982 (16.09%)	32,594 (3.19%)	0.45	981 (16.07%)	965 (15.81%)	0.01
Alcohol dependence	264 (4.33%)	8255 (0.81%)	0.22	263 (4.31%)	198 (3.24%)	0.06

DM dermatomyositis, *BMI* body mass index

The assessed baseline characteristics among dermatomyositis patients and controls are described. Each cohort underwent 1:1 propensity score matching analysis to balance each cohort by demographics (age, sex, and race) and comorbidities (diabetes mellitus, essential hypertension, chronic lower respiratory disease, chronic kidney disease, nicotine dependence, alcohol dependence, heart failure, ischemic heart disease, body mass index, and neoplasms)

however, the statistically significant rise in 60-day vaccine adverse events may be attributed to autoimmunity being triggered or change in immunosuppressive treatment in patients with autoimmune diseases, a finding that has also been suggested by previous reports [8]. Nevertheless, the benefits of getting vaccinated greatly outweigh the risks in this population especially given very small absolute percent risk [9]. Limitations of this study include potential errors in coding entry and an inability to determine DM severity at time of vaccination. We hope that future studies like the ongoing COVAD study address this gap [10].

While DM patients experienced higher adverse events compared to matched non-DM patients, these findings should not be a deterrent against vaccination in most cases as overall risk for ACH, BI, or immediate anaphylaxis was not increased. Temporal trends of rising AESI at 60 days call for further studies to explore long-term impacts of vaccination in DM patients, especially given high thrombogenic risk associated with DM. Moreover, increasing trends of all-cause hospitalization in DM patients is a concern and additional data is needed with a specific focus on flares of underlying DM.

Abbreviations ACH: All-cause hospitalization; BI: Breakthrough infection; DM: Dermatomyositis; RR: Relative risk; AESI: Adverse events of special interest; CDC: Centers for Disease Control and Prevention; FDA: Food and Drug Administration

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10067-022-06081-7.

Declarations

Disclosures None.

References

1. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Pérez Marc G, Moreira ED, Zerbini C, Bailey R, Swanson KA, Roychoudhury S, Koury K, Li P, Kalina WV, Cooper D, Frenck RW Jr, Hammitt LL, Türeci Ö, Nell H, Schaefer A, Ünal S, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU, Gruber WC (2020) Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. N Engl J Med 383(27):2603–2615. https://doi.org/10.1056/NEJMoa2034577

Table 2 Post-vaccination 1-day, 30-day, and 60-day outcomes in patients with a diagnosis of dermatomyositis compared to non-inflammatory myositis controls before and after propensity matching for baseline characteristics. Data is listed as percentage (number) and relative risk (95% confidence interval)

Outcomes	Before propensity matching					After propensity matching				
	Vaccinated DM ($N=6104$)	Vaccinated non-DM ($N=1,022,471$)	Risk ratio (95% CI)	Risk difference (95% CI)	*P*-value	Vaccinated DM ($N=6103$)	Vaccinated non-DM ($N=6103$)	Adjusted risk ratio (95% CI)	Adjusted risk difference (95% CI)	*P*-value
1-day outcome										
Immediate adverse event	0.4% (27/6104)	0.1% (553/1022471)	8.18 (5.56, 12.03)	0.39% (0.22%, 0.55%)	< 0.001	0.4% (27/6103)	0.2% (15/6103)	1.80 (0.96, 3.38)	0.20% (− 0.01%, 0.4%)	0.064
30-day outcomes										
Adverse events of special interest*	≤ 10/4325	0.1% (960/965249)	NA[a]	NA[a]	NA[a]	≤ 10/4325	≤ 10/4829	NA[a]	NA[a]	NA[a]
COVID breakthrough infection[†]	0.7% (41/5636)	0.2% (1990/985300)	3.60 (2.65, 4.9)	0.53% (0.3%, 0.75%)	< 0.001	0.7% (41/5635)	0.5% (29/5734)	1.44 (0.90, 2.31)	0.22% (− 0.07%, 0.51%)	0.13
All-cause hospitalization	1.6% (97/6104)	0.4% (4315/1022471)	3.77 (3.08, 4.6)	1.17% (0.85%, 1.48%)	< 0.001	1.6% (97/6103)	1.5% (92/6103)	1.05 (0.79, 1.40)	0.08% (− 0.36%, 0.52%)	0.71
60-day outcomes										
Adverse events of special interest*	0.6% (28/4325)	0.2% (1780/965249)	3.51 (2.42, 5.09)	0.46% (0.22%, 0.7%)	< 0.001	0.6% (28/4325)	0.3% (16/4834)	1.96 (1.06, 3.61)	0.32% (0.03%, 0.61%)	0.029
COVID breakthrough infection[†]	0.8% (46/5636)	0.2% (2442/985300)	3.29 (2.46, 4.4)	0.57% (0.33%, 0.8%)	< 0.001	0.8% (46/5635)	0.7% (38/5725)	1.23 (0.80, 1.89)	0.15% (− 0.16%, 0.47%)	0.34
All-cause hospitalization	2.9% (177/6104)	0.7% (7629/1022471)	3.89 (3.36, 4.5)	2.15% (1.73%, 2.57%)	< 0.001	2.9% (176/6103)	2.7% (162/6103)	1.09 (0.88, 1.34)	0.23% (− 0.35%, 0.81%)	0.44

*Patients with a prior history of an adverse event of special interest were excluded from this analysis

†Patients with a prior history of a COVID-19 infection were excluded from this analysis

[a] "NA" indicates not enough patients to determine relative risk and risk difference due to sample size ≤ 10

CI confidence interval, *DM* dermatomyositis

The assessed vaccination outcomes among DM patients and controls are described. Each cohort underwent 1:1 propensity score matching analysis to balance each cohort by demographics (age, sex, and race) and comorbidities (diabetes mellitus, essential hypertension, chronic lower respiratory disease, chronic kidney disease, nicotine dependence, alcohol dependence, heart failure, ischemic heart disease, body mass index, and neoplasms)

2. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Creech CB, McGettigan J, Khetan S, Segall N, Solis J, Brosz A, Fierro C, Schwartz H, Neuzil K, Corey L, Gilbert P, Janes H, Follmann D, Marovich M, Mascola J, Polakowski L, Ledgerwood J, Graham BS, Bennett H, Pajon R, Knightly C, Leav B, Deng W, Zhou H, Han S, Ivarsson M, Miller J, Zaks T (2021) Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 384(5):403–416. https://doi.org/10.1056/NEJMoa2035389
3. Sadoff J, Le Gars M, Shukarev G, Heerwegh D, Truyers C, de Groot AM, Stoop J, Tete S, Van Damme W, Leroux-Roels I, Berghmans PJ, Kimmel M, Van Damme P, de Hoon J, Smith W, Stephenson KE, De Rosa SC, Cohen KW, McElrath MJ, Cormier E, Scheper G, Barouch DH, Hendriks J, Struyf F, Douoguih M, Van Hoof J, Schuitemaker H (2021) Interim results of a phase 1–2a trial of Ad26COV2S COVID-19 vaccine. N Engl J Med 384(19):1824–1835. https://doi.org/10.1056/NEJMoa2034201
4. Boekl L, Kummer LY, Dam KPJV, Femke H, Kempen ZV, Vogelzang EH, Wieske L, Eftimov F, Vollenhoven RV, Kuijpers TW, Ham SMV, Tas SW, Killestein J, Boers M, Nurmohamed MT, Wolbink TRG (2021) Adverse events after first COVID-19 vaccination in patients with autoimmune diseases. The Lancet Rheumatol 3(8):E542–E545. https://doi.org/10.1016/S2665-9913(21)00181-8
5. Hadi YB, Thakkar S, Shah-Khan SM, Hutson W, Sarwari A, Singh S (2021) COVID-19 vaccination is safe and effective in patients with inflammatory bowel disease: analysis of a large multi-institutional research network in the United States. Gastroenterol 161(4):1336-1339.e3. https://doi.org/10.1053/j.gastro.2021.06.014
6. Saud A, Naveen R, Aggarwal R, Gupta L (2021) COVID-19 and myositis: what we know so far. Curr Rheumatol Rep 23(8):63. https://doi.org/10.1007/s11926-021-01023-9
7. Khan S, Gasparyan AY, Gupta L (2021) Lessons learned from publicizing and retracting an erroneous hypothesis on the mumps, measles, rubella (MMR) vaccination with unethical implications. J Korean Med Sci 36(19):e126. https://doi.org/10.3346/jkms.2021.36.e126
8. Barbhaiya M, Levine JM, Bykerk VP, Jannat-Khah D, Mandl LA (2021) Systemic rheumatic disease flares after SARS-CoV-2 vaccination among rheumatology outpatients in New York City. Ann Rheum Dis 80(10):1352–1354. https://doi.org/10.1136/annrheumdis-2021-220732
9. Tariq J, Gupta L (2021) Safety and efficacy of COVID-19 vaccines in pregnant women with rheumatic diseases: an immunologic perspective. Rheumatol Int 41:1545–1547. https://doi.org/10.1007/s00296-021-04918-z
10. Sen P, Gupta L, Lilleker JB, Aggarwal V, Kardes S, Milchert M, Gheita T, Salim B, Velikova T, Gracia-Ramos AE, Parodis I, O'Callaghan AS, Nikiphorou E, Tan AL, Cavagna L, Saavedra MA, Shinjo SK, Ziade N, Knitza J, Kuwana M, Cagnotto G, Nune A, Distler O, Chinoy H, Aggarwal V, Aggarwal R (2022) COVID-19 vaccination in autoimmune disease (COVAD) survey protocol. Rheumatol Int 42(1):23–29. https://doi.org/10.1007/s00296-021-05046-4